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Gynecology

A STUDY OF EPIDEMIOLOGIC FACTORS IN CARCINOMA OF THE UTERINE CERVIX*

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ETIOLOGICAL factors in carcinoma of the uterine cervix are unknown. Its prevalance in married women is considerably greater than in the unmarried, with a further excess in parous individuals. The relative incidence in Gentile and Jewish women is approximately 8:1. Previous studies have suggested also that marriage before the age of 20, divorce or separation, birth of the last child before the age of 25, syphilis, lacerations of the cervix, douching with cold tar derivatives, contraceptives, lack of circumcision of the husband, and poverty are factors of significance in the development of carcinoma of the cervix.[1, 2, 3, 7]

These studies indicated two possible reasons for excessive exposure to the extrinsic factors; either poverty forces this association, as in other chronic diseases, or some endogenous difference in hormone levels induces a greater desire for early marriage and childbearing. In support of the latter, Ayre[4] has claimed that vaginal cytologic studies show an unusually high estrogen level in women with carcinoma of the cervix. Experimentally, Gardner[5] produced cancer of the cervix in inbred strains of mice by injecting large doses of estrogen.

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Materials and Methods

In order to test the validity of these relationships a study was designed to determine association of exogenous and endogenous factors with the disease. The study was divided into two phases, both for patients with the neoplasm and for controls: skilled interviewers using a detailed protocol, and studies of urinary excretion of estrogens.

The entire pattern of the interview, as well as its areas of inquiry and an impressive number of individual items, was determined during periodic, lengthy conferences between the authors, Professor Elizabeth E. Payne of the School of Social Work, and a biostatistician from the Bureau of Chronic Diseases. Factors previously reported as having any possible association with cervical carcinoma were included, and additional items were developed from a thorough consideration of all possible facets derived from certain associations generally regarded as highly significant, as follows:*

1. The relative infrequency of cancer of the cervix in Jewish women. This suggested dietary factors, the hygienic code of orthodox Jews, or the commonly implicated factor of lack of circumcision as logical items for inquiry.

2. The greater incidence of cancer in parous women. This required investigation of events surrounding conception, the course of pregnancy and parturition and postparturition, including diet, hygiene, infections, trauma, bleeding, and sexual relations.

3. The lack of carcinoma of the cervix in nuns as reported by Gagnon.[6] This implicated sexual patterns, hygienic care, i.e., douching practices and contraceptives, as factors for survey in the environmental background of cancer of the cervix.

"*Cases*" were patients with invasive primary squamous carcinoma of the uterine cervix, verified by histologic examination in every instance. Preinvasive (Stage 0) lesions were excluded, as were adenocarcinomas.

Controls were patients from the same sources as the cases, without gynecologic disease or cancer of any site (except of the skin), by quinquennial period of age, and with the same distribution of race and parity.

To assure some degree of contrast in economic background, the samples were obtained from two sources, the Los Angeles County Hospital and private practice. After 4 years, the study ended with 429 cases of cervical carcinoma and 429 matched controls. At the County Hospital 274 cases and an equal group of controls were interviewed, a sample selected by the criterion of "medical indigency" as a requisite for admission. From private practice (almost entirely from one office), 155 cases and 155 controls voluntarily agreed to participate after the nature of the interview had been outlined. The County Hospital and private practice subjects are referred to hereafter as "ward" and "private," respectively. The ratio of ward to private, for both cases and controls, was approximately 1.8 to 1.0.

An attempt was made to interview every diagnosed case during the project, but on a volunteer basis. Those who refused, or could not be interviewed because of debility, were listed. The number of refusals among the cases and controls was comparable. Additional economic controls within the protocol were adequacy of housing, education of the patient before marriage, occupation of the father, and an estimation of the father's actual income.

*Pretesting of the interview protocols was done by Professor Payne; some nonproductive items were eliminated, changes in format and sequence were made.

Interview Method

The interviews were conducted by experienced, graduate social workers, of whom there were three during the project. As indicated earlier, a faculty representative assisted in the planning phase for the School of Social Work, and Professor Payne followed this contribution by obtaining a leave of absence to do the first year of interviewing. She provided also a thorough indoctrination of her successors, and was available for consultation as needed.* Each worker matched her own cases and controls. The interview method was that which is standard for social work. This involves an invitation to the patient to volunteer information in one sphere of the interview, followed by specific questioning of areas not answered exactly.

The questioning included not only when events occurred, but why they occurred. For example: "Why did you get married?" "Where did you learn about douching?" "Why do you douche?" The marital history included not only how often intercourse occurred, but whether the patient desired it and was satisfied by it. By illustration, here are some of the instructions for the questionnaire on douching: "Douching refers to flushing the vaginal canal with water (with or without medication): Ask: 'Do you douche at the time of your period? Or at any time during your bleeding, or just after it is over?' We ask these questions because we honestly do not know whether douching at this time protects or may possibly harm the health of the cervix. So, if we learn what is done, we may get an answer to that question." The scope of this section included first douching and first source of information, douching post coitus, frequency of douching, age at which she stopped, materials and amounts used, duration of use of each, temperature of fluid, apparatus and type used, how and where kept, other uses for the douching apparatus, whether she was sole user.

The detail of the questionnaire will explain why each interview lasted between 2 and 3 hours, and the total study extended over a period of 4 years. The social workers had no specific previous experience with medical problems, therefore they had no preconceived idea as to how the interview questions should be answered. Their only summation of the interview experience at the end of the study was that they were quite impressed by the similarity of the responses from the cases and controls. This is of special interest, because the questions of more subjective content (the "why" questions) showed differences between cases and controls; these differences were uniform in the groups studied by each social worker. There were two samplings of results before the final summary, but the social workers were not allowed to see any of these data in order that their further interviews would not be prejudiced.†

Results

This preliminary outline of results of this study, to be complemented by more detailed reports in other journals, will describe briefly the data relating to several phases of the investigation:

Nutritional factors
Socioeconomic background
Estimation of psychic-physical stress
Urinary excretion pattern of estrogens

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*We are indebted also to Virginia Conrad and Gwendolyn Blanchard for their highly competent and faithful work as interviewers. Statistical analyses of randomized samples verified the reliability of all three interviewers.

†A study of similar design to ours but employing different interview techniques was reported by Wynder and associates[7] in 1954.

Nutritional Factors.—A protocol for the detection of deficiencies of thiamine and riboflavin was formulated and approved by nutritionists of the University of California and the University of Southern California.* Table I shows the specific groups investigated. The patient's ability to remember the essential foods eaten before and after age 18 seemed good. There were no significant differences in total thiamine and riboflavin intake between cancer cases and controls at any age period.

TABLE I. FOOD GROUPS, CONSUMPTION OF WHICH SERVED AS A BASIS FOR ESTIMATION OF THIAMINE AND RIBOFLAVIN

1. Meat
2. Beans
3. Sweet potatoes
4. Cooked cereal, other cereals
5. Bread
6. Green vegetables
7. Organ meats
8. Eggs
9. Milk
10. Yellow cheese

Other factors studied which might suggest differences in estrogen metabolism, namely, alcohol intake, mastodynia, onset of menarche, onset of menopause, and irrgeularity of menses, showed no significant differences between cases and controls. Table II demonstrates that menstrual irregularities were frequent but equal among both cancer cases and controls. This sort of evidence gave no indication that estrogen levels were different between cases and controls.

TABLE II. MENSTRUAL IRREGULARITIES

	CASES (%)	CONTROLS (%)
Menorrhagia	38	46
Variation in menstrual pattern		10
No variation	11	
Nonmenstrual bleeding	24	24

Socioeconomic Background.—In the study of hygienic factors the orthodox Jewish practices are of much interest, because in the Code there is no provision for douching. Menses must be followed by abstinence from coitus for 7 days. Pregnancy is followed by abstinence for about 40 days. Our questions, therefore, attempted to find out whether coitus and douching occurred with, or only after, menses. The tabulation showed that types of douching materials (including coal tar derivatives), frequency of douching, apparatus used, and total years of douching did not differ significantly between cases and controls. The amount of bathing by cases and controls, and by their partners, showed no significant differences.

Circumcision of the marital partner has been claimed by some workers to be the most important difference between cervix cancer cases and controls. Our interviews showed that circumcision of the first husband, or partner of longest duration, was equally frequent in cases and controls when the Jewish patients were eliminated from the study (Table III). The data were enough different from previously published reports that our collaborating statisticians rematched cases and controls by various techniques of regrouping. All

*Professor Ernest Geiger, Department of Biochemistry and Nutrition, University of Southern California, was special consultant.

approaches verified the initial conclusion, namely, that circumcision, or lack of circumcision, was as frequent in partners of cases with cancer as in the partners of controls.*

TABLE III. CIRCUMCISION OF PARTNER KNOWN LONGEST. CERVICAL CANCER AND CONTROL PATIENTS MATCHED ON AGE

	CIRCUMCISION OF PARTNER		
	NO (%)	YES (%)	UNKNOWN (%)
Ward patients, white			
Cases	60	29	
Controls	68	27	
Private patients, white			
Cases	56	37	
Controls	60	39	
Ward patients, Negro			
Cases	47	35	
Controls	59	32	
Total patients			
Cases			11
Controls			6

Data were collected concerning frequency of coitus, duration of total marital state, years with first husband, total number of permanent partners, and total number of casual partners. In the beginning of the interview the patients had been told that information of a very personal nature would be needed. The items required for a pattern of sexual activity were placed toward the close of the interviews, and each of the workers felt that this part of the interview was quite reliable; most of the patients indicated a near-total recall of such intimate areas. There were no significant differences found between cases and controls in any of the items related to sexual practices (Tables IV, V, VI).

TABLE IV. TOTAL YEARS OF MARRIAGE FOR MOST OF THE CANCER CASES AND CONTROLS. THERE IS NO SIGNIFICANT DIFFERENCE IN THE TWO GROUPS

NUMBER OF YEARS OF MARITAL AND/OR NONMARITAL RELATIONS	CASE (%)	CONTROL (%)
10-20 years	31	30
20-40 years	49	48

TABLE V. PART OF THE DATA ON FREQUENCY OF COITUS. AT AGES LESS THAN 30, AS AT OTHER AGES, THE FREQUENCY WAS SIMILAR IN THE TWO GROUPS

FREQUENCY OF COITUS AT AGES LESS THAN 30	CASES (%)	CONTROLS (%)
4 or more times a week	33	32
1-3 times a week	57	56

TABLE VI. NUMBER OF CASUAL (LESS THAN 6 MONTHS) SEXUAL PARTNERS*

NO. OF PARTNERS	CASES (%)	CONTROLS (%)
Less than 5	18	19
More than 5	8	8

*Previous reports have held that cancer patients have more casual sexual partners. Table VI shows that in our group there was no significant difference between cancer cases and controls.

In contrast to the preceding data, when questions were asked about general health, such items as colds, infections, weight gains and losses were not well remembered.

*Details of these matching procedures, and statistical validation of other conclusions reported herein will appear in a pending publication by John S. Dunn, Jr., M.D.

Many items related to pregnancies were included: types and number of pregnancies, hygiene and coitus during pregnancy, manner of delivery (attended and unattended, with or without instruments), and bleeding or infection after pregnancy. No significant differences between cases and controls were discoverable (Table VII). Questions about cervical lacerations were found unreliable, as the patients only knew about stitches after delivery.

TABLE VII. MANNER OF DELIVERY

	CASES (%)	CONTROLS (%)
Without medical attention at termination of pregnancy	15	15
Deliveries by forceps	17	23

There was a significant excess among the cases with carcinoma of first pregnancy before age 20 and birth of last child before age 25, as well as marriage before age 20 (Tables VIII, IX), and separation and divorce.

TABLE VIII. AGE AT FIRST MARRIAGE IN WHITE PATIENTS WITH CERVICAL CANCER AND CONTROLS MATCHED ON AGE

	19 OR EARLIER (%)	20 OR LATER (%)	TOTAL NO.
Ward.—			
Cases	66	34	153
Standardized controls	56	44	153*
Private.—			
Cases	42	58	149
Standardized controls	35	65	149*
Total.—			
Cases	54	46	302
Standardized controls	45	55	302*

*Equivalent number after age standardization.

TABLE IX. MEAN AGE AT FIRST MARRIAGE IN WHITE PATIENTS WITH CERVICAL CANCER AND CONTROLS MATCHED ON AGE

	WARD				PRIVATE			
	CASES		CONTROLS		CASES		CONTROLS	
AGE OF PATIENT	NO.	MEAN AGE AT FIRST MARRIAGE	NO.	MEAN AGE AT FIRST MARRIAGE	NO.	MEAN AGE AT FIRST MARRIAGE	NO.	MEAN AGE AT FIRST MARRIAGE
-34	17	17.35	11	20.45	10	19.20	14	21.64
35-44	35	18.11	41	21.45	31	22.39	42	22.25
45-54	28	17.54	32	19.28	63	20.66	46	22.82
55-64	30	20.29	24	21.92	34	21.97	24	23.37
65-74	29	19.28	30	21.53	11	21.72	10	24.10
75 and over	14	20.57	13	24.08	1	22.00	No control	
Total	153		151		150		136	

In Table IX it is seen that this same relationship holds true when the patients are separated by age groups at time of interview.

All estimates of economic background showed lower standards of living among the ward cancer patients. This was also true of the private cancer patients (Tables X, XI). A cross control was run of age at first marriage against the different economic levels as indicated by education, occupation of father, and degree of crowding in the house. With this control obviating the factor of relative poverty, and early marriage as a constant variable, the latter factor remained more prominent in the social background of cases than of controls (Tables XII, XIII).

TABLE X. AGE AT FIRST MARRIAGE BY OCCUPATION GROUP OF FATHER, WHITE PATIENTS WITH CERVICAL CANCER AND CONTROLS MATCHED ON AGE

	WHITE COLLAR*			MANUAL WORKER*			FARMER*		
	AGE AT FIRST MARRIAGE			AGE AT FIRST MARRIAGE			AGE AT FIRST MARRIAGE		
	−19 (%)	20+ (%)	TOTAL NO.	−19 (%)	20+ (%)	TOTAL NO.	−19 (%)	20+ (%)	TOTAL NO.
Ward.—									
Cases	57	43	35	65	35	63	63	37	51
Standardized controls	49	51	35†	57	43	63†	55	45	51†
Private.—									
Cases	40	60	57	41	59	41	44	56	50
Standardized controls	30	70	57†	37	63	41†	38	62	50†
Total.—									
Cases	47	53	92	56	44	104	53	47	101
Standardized controls	38	62	92†	49	51	104†	47	53	101†

*There were 7 cases and 16 controls whose fathers' occupations were not stated.
†Equivalent number after age standardization.

TABLE XI. EDUCATION OF PATIENT, WHITE PATIENTS WITH CERVICAL CANCER AND CONTROLS MATCHED ON AGE

	11 GRADES OR LESS*			12 GRADES OR MORE		
	AGE FIRST MARRIAGE			AGE FIRST MARRIAGE		
	−19 (%)	20+ (%)	TOTAL NO.	−19 (%)	20+ (%)	TOTAL NO.
Ward.—						
Cases	71	29	113	50	50	38
Standardized controls	60	40	113†	50	50	38†
Private.—						
Cases	57	43	76	27	73	70
Standardized controls	53	47	76†	21	79	70†
Total.—						
Cases	65	35	189	35	65	108
Standardized controls	57	43	189†	31	69	108†

*For those with less education, difference significant at 0.05 level for Ward Group only.
†Equivalent number after age standardization.

TABLE XII. FATHER'S OCCUPATION, WHITE PATIENTS WITH CERVICAL CANCER AND CONTROLS MATCHED ON AGE

	WHITE COLLAR* WORKER (%)	MANUAL† WORKER (%)	TOTAL NO.	NO OCCUPATION OR UNKNOWN (NO.)
Ward.‡—				
Cases	23	77	149	4
Standardized controls	34	64	149§	9
Private.‡—				
Cases	38	62	146	3
Standardized controls	44	56	146§	3

*Includes professionals, managers, officials, and proprietors.
†Includes craftsmen, foremen, semiskilled workers, laborers, and farmers.
‡Difference significant at 0.05 level in private group; 0.01 level in ward group.
§Equivalent number after age standardization.

When the factor of separation and divorce was cross controlled by age groups it was apparent that separation and divorce were frequent among both cases and controls who had married early. Among the cases there were more separation and divorce in those marrying after age 20 than in the comparable control groups (Table XIV). In common with other findings here reported, we discern no easy answer to these differences.

The greater incidence of carcinoma in Gentiles over Jews was again noted.

The greater incidence in women with syphilis was apparent; 7 per cent of the cases had clear-cut evidence of syphilis, only 4 per cent of the control group.

TABLE XIII. EDUCATION, WHITE PATIENTS WITH CERVICAL CANCER AND CONTROLS MATCHED ON AGE

	11 GRADES OR LESS (%)	12 GRADES OR MORE (%)	TOTAL NO.	NO. NOT STATED
Ward.—				
Cases	75	25	151	2
Standardized controls	71	29	151*	2
Private.—				
Cases	52	48	146	3
Standardized controls	43	57	146*	3
Total.—				
Cases	64	36	297	5
Standardized controls	57	43	297*	3

*Equivalent number after age standardization.

TABLE XIV. NUMBER OF DIVORCES AND SEPARATIONS BY AGE AT FIRST MARRIAGE, WHITE PATIENTS WITH CERVICAL CANCER AND CONTROLS MATCHED ON AGE

	MARRIED BEFORE AGE 20*			MARRIED AGE 20 OR LATER†		
	NUMBER OF DIVORCES AND SEPARATIONS			NUMBER OF DIVORCES AND SEPARATIONS		
	0 (%)	1+ (%)	TOTAL NO.	0 (%)	1+ (%)	TOTAL NO.
Ward.—						
Cases	39	61	101	54	46	52
Standardized controls	44	56	101‡	56	44	52‡
Private.—						
Cases	38	62	63	66	34	87
Standardized controls	40	60	63‡	77	23	87‡
Total.—						
Cases	38	62	164	61	39	139
Standardized controls	42	58	164‡	69	31	139‡

*None of the differences significant at 0.05 level.
†Differences significant for private group at 0.01 level, and for total group at 0.02 level.
‡Equivalent number after age standardization.

Estimation of Psycho-physical Stress.—The more subjective parts of the interview as to why marriage occurred, satisfaction of coital relations, and the stability of the home suggested that there were conditions other than poverty alone which encouraged early marriage and contributed to separation and divorce (Tables XV, XVI). Dissatisfaction or discontent with the home situation, domestic insecurity, and unstable marital relationships were reported with greater frequency by cases than by controls. The summation of these largely intangible considerations was estimated for each individual in terms of degrees of stress of living experienced since childhood for variable periods of time. The patients with cervical carcinoma were consistently estimated as having been under more stressful conditions, and for greater portions of their lives, than their matched controls. This subjective estimate of stress, reported in excess for cancer cases by all three of the social workers involved in the study, was subjected to statistical testing for validity. Both by criteria applied to the three individual samples and by cross-testing of each investigator's ratings against the others, the consistency of the case-control difference was valid.

TABLE XV. REASON FOR FIRST MARRIAGE, SEEN TO BE ON A MORE STABLE EMOTIONAL BASIS AMONG THE CONTROL PATIENTS

	CASES (%)	CONTROLS (%)
Love	44	53
Dissatisfied with living arrangement	20	13
Other	28	28

TABLE XVI. SEXUAL GRATIFICATION

	NO (%)	YES (%)	VARIED (%)
With First Partner.—			
Cases	54	44	
Controls	37	60	
Throughout Sexual Life.—			
Cases	33	37	27
Controls	23	57	19

Urinary Excretion Pattern of Estrogens.—Estrogen determinations were performed on 24 hour urine specimens. The urinary estrogens were fractionated by the procedure of Engel,[10] and the estrogen-containing phenolic extract was further analyzed by means of a 24 tube countercurrent distribution. The relative amounts of estrogen present were determined by fluorescent measurement.

Results of the countercurrent distribution of the urinary estrogen fraction showed the presence of two major fluorogenic components, namely, the E-0 and E-3 fractions. Designation of each fraction was made on the basis of their relative position in the countercurrent distribution, and, therefore, the E-0 fraction was mainly in the 0 and 1 tubes of the distribution, while the position of the E-3 component was similar to the position of estriol. Since the partition coefficients of these two components differed greatly in the solvent system employed, a 5 tube distribution with complete stripping was used to separate them. Subsequently each fraction was analyzed by fluorescent measurement.

The individual values of the E-0 and E-3 fractions from 72 patients were evaluated to determine whether there was a correlation of each component with the presence of cervical carcinoma. No association was evident in the examination of the individual values of these two components and the extent or type of disease. When the ratio of the E-3 to E-0 fractions was compared, however, the E-3/E-0 ratio was greater only in the postmenopausal women with cervical carcinoma than in the corresponding control group (Table XVII).

TABLE XVII. COMPARISON OF THE E-3/E-0 RATIOS OF THE CONTROL GROUP AND THE PATIENTS WITH CERVICAL CARCINOMA*

GROUP OF PATIENTS	NO. OF PATIENTS	E-3/E-0 VALUES	P VALUE†
Premenopausal.—			
Controls	20	2.37/0.46‡	0.20
Carcinoma of cervix	18	2.09/0.82	
Postmenopausal.—			
Controls	17	1.97/0.42	0.01
Carcinoma of cervix	17	3.14/1.30	
Controls.—			
Premenopausal	20	2.37/0.46	0.01
Postmenopausal	17	1.97/0.42	

*Dr. James Demetriou, Department of Biochemistry, performed all the determinations.
†Probabilities of differences in the means as determined by the Fisher "t" test.
‡Standard error of the mean.

Summary

We believe that this epidemiologic study of carcinoma of the cervix uteri has been carefully controlled, and that the reliability of the data has been demonstrated. The specific items of importance which have been under scrutiny are: dietary deficiency, estrogen excretion levels, menstrual patterns, hygienic practices, contraceptives, circumcision of marital and other partners, and frequency and duration of coitus; for none of these items was there any significant difference between the cases and their matched controls. There is some evidence to show that a constellation of factors related to socioeconomic conditions and domestic and marital instability are more prominent in women who have carcinoma of the cervix than in comparable groups without this disease. The study, therefore, does not disclose any new, specific causative factor for uterine cervical carcinoma. It does re-emphasize the importance of the socioeconomic complex of relative poverty (at least in early life) with rapid maturation sexually and a haste to begin early, and early to terminate, the reproductive phase of biologic destiny—marriage, intercourse, first and last pregnancies, separation, divorce—all of these events occur significantly earlier in the life of the woman destined to develop uterine cervical carcinoma than in the woman without this disease, in similar age distributions.

The basic phenomena underlying these dissimilarities of cancer patient and "control" are not apparent, yet they may constitute factors of determinative importance in the genesis of this neoplasm. Any promising approach toward their elucidation should be prosecuted intensively, and with some considerable promise of discoveries important in other analogous *genital* neoplasms.

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CONSTITUTIONAL STIGMAS ASSOCIATED WITH ENDOMETRIAL CARCINOMA*

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CLINICAL investigators frequently have commented on a constitutional predisposition to endometrial carcinoma. These coincidental peculiarities may be of both etiological and diagnostic significance. Way[1] has suggested a hereditary predisposition to the prolonged overactivity of the anterior pituitary gland as an etiological factor of primary importance. Such overactivity of the pituitary gland might well explain certain of the commonly noted clinical characteristics of patients with carcinoma of the endometrium.

Clinical stigmas said to be associated with carcinoma of the endometrium include obesity, hypertension, altered carbohydrate metabolism with tendencies toward diabetes, infertility, late occurrence of the menopause, hyperplasia of the endometrium, and irregular bleeding at the time of the menopause. According to the hypothesis propounded by Way, the prolonged overactivity of the anterior pituitary gland could influence carbohydrate metabolism with resultant obesity and hypertension, and ultimately decreased carbohydrate tolerance and clinical diabetes. Prolonged and excessive stimulation of the ovaries and the adrenal glands might also produce endometrial hyperplasia, infertility, the delayed onset of the menopause, and irregular bleeding at the time of the menopause.

The reported high incidence of concurrent endometrial carcinoma and diabetes mellitus has stimulated this further investigation. Scheffey and Thudium,[2] in a study of 127 cases of endometrial carcinoma, reported an 11 per cent incidence of associated diabetes. Palmer, Reinhard, Sadugor, and Goltz[3] in a similar study of 165 cases found a 16.9 per cent incidence of diabetes. Hertig and Sommers[4] reported diabetes in 9 per cent of their cases of endometrial carcinoma. Moss,[5] in 1947, made a detailed study of 23 consecutive cases of endometrial carcinoma and found approximately two thirds of these patients to have abnormal glucose tolerance curves of the diabetic type. Glicksman and Rawson,[6] studying 638 patients with all forms of cancer, found the glucose tolerance tests to be of the diabetic type in 36.7 per cent. Of the 25 patients with endometrial carcinoma, there was a 64 per cent incidence of abnormal glucose tolerance. Peel[7] pointed out the wide discrepancies quoted in the

*Presented at a meeting of the Obstetrical Society of Philadelphia, Oct. 3, 1957.

literature of concomitant endometrial carcinoma and diabetes. These reported incidences vary from 1.2 to 29 per cent. Spiegelman and Marks,[8] in 1946, in a survey of 1,300,399 women over 35 years of age, reported a 1.02 per cent incidence of diabetes. This study was based on the results of single fasting blood sugar determinations. A further survey of the available literature fails to give evidence of studies utilizing an adequate control group in which identical laboratory investigations and clinical comparisons have been made of patients with and without endometrial carcinoma.

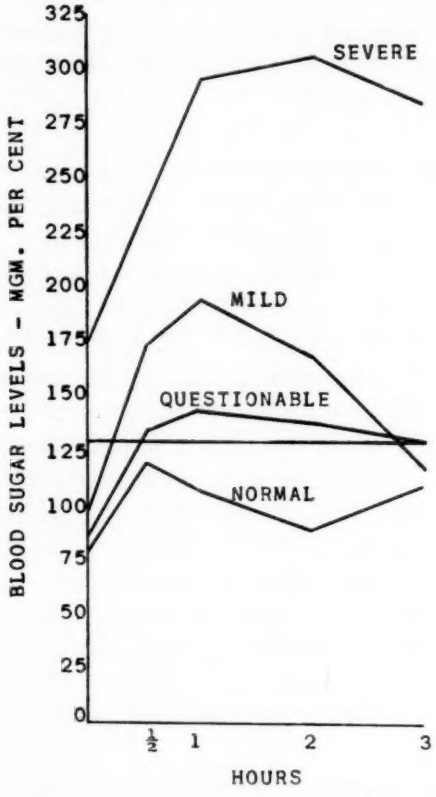

Fig. 1.—Typical glucose tolerance curves from this study.

Material

The sources of material for this study were the Division of Obstetrics and Gynecology of the Pennsylvania Hospital, the Benjamin Franklin Clinic of the Pennsylvania Hospital, and the Department of Gynecology of the Graduate Hospital of the University of Pennsylvania. Glucose tolerance tests were performed on 50 random patients with proved endometrial carcinoma, both treated cases as seen in the special tumor follow-up clinic and new cases as they were admitted to the hospital. For purposes of comparison a control group of 50 women in the Benjamin Franklin Diagnostic Clinic were similarly examined for glucose tolerance. The patients in the control group were all 40 years of age or older in whom pre-existing diabetes was unknown, and none had endometrial carcinoma. A third group of 12 women, in all of whom a histologic diagnosis of atypical or adenomatous hyperplasia of the endometrium

had been made, were likewise studied for glucose tolerance. The patients in all three groups were analyzed in regard to age, obesity, parity, hypertension, and age at the menopause.

Method

For the determination of glucose tolerance, the standard 3 hour oral glucose tolerance test, with 100 Gm. of glucose in 300 c.c. of water, was utilized. Venous blood sugar levels were determined by the Folin-Wu method. An initial fasting blood sugar determination was made just prior to the ingestion of the measured amount of glucose solution. Further blood sugar levels were determined at ½, 1, 2, and 3 hour intervals. Urine specimens were examined at these same intervals for the presence of glucose.

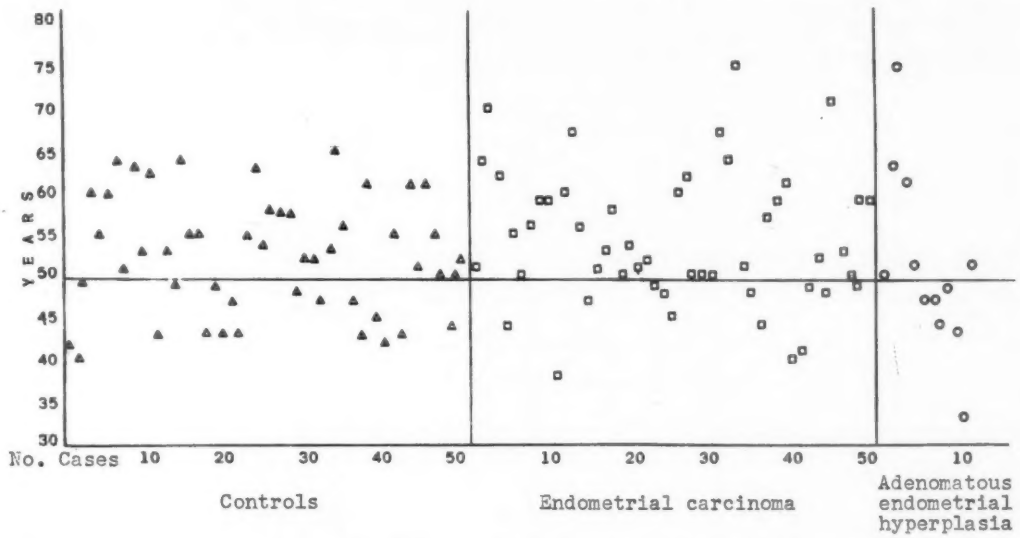

Fig. 2.—Distribution of patients according to age in the control series and in the groups with endometrial carcinoma and adenomatous endometrial hyperplasia.

Duncan[9] stated that the standard 3 hour oral glucose tolerance test is the most exacting and, when properly evaluated, the test of choice for determining, in doubtful cases, the presence or absence of diabetes. The value of this test lies in its diagnostic aid and not as an indicator of the severity of the diabetes. Carbohydrate tolerance is influenced unfavorably during the course of infections, hepatic disturbances, and dietary restrictions, especially a starvation regimen or a low carbohydrate diet. Such conditions cause temporary alterations in glucose tolerance which are adaptations to a reduced demand for insulin. These complicating factors were avoided as carefully as possible in this study.

Glucose tolerance curves were considered indicative of diabetes if the fasting blood sugar level exceeded 120 mg. per cent or if the 2 hour value exceeded 130 mg. per cent.[9] When the diabetes is of a mild nature the fasting blood sugar may be normal, while the 2 hour specimen is elevated. This determination is of the greatest importance as a diagnostic aid in the detection of diabetes mellitus. The interpretation of glucose tolerance in this study is based on these criteria.

Fig. 1 shows four typical glucose tolerance curves taken from the study. In the normal curve both the fasting and the 2 hour blood sugar levels are

within the normal range. In the questionable curve and the mildly diabetic curve the fasting levels are within the normal range, but the 2 hour determinations are elevated above 130 mg. per cent. The curve which is indicative of unquestionable and possibly severe diabetes shows a fasting level well above 120 mg. per cent, and a 2 hour level which is greatly elevated.

The other factors including age, obesity, parity, hypertension, and age at the menopause were studied by clinical comparison of the three groups.

Results

Age.—Study of the age groups as shown in Fig. 2 indicates that the three categories of patients are comparable. In both the control group and the endometrial carcinoma group approximately one third of the patients were under 50 years of age, and the other two thirds were 50 years of age or older. Of the 12 patients who had adenomatous endometrial hyperplasia, a relatively larger number were in the younger age group.

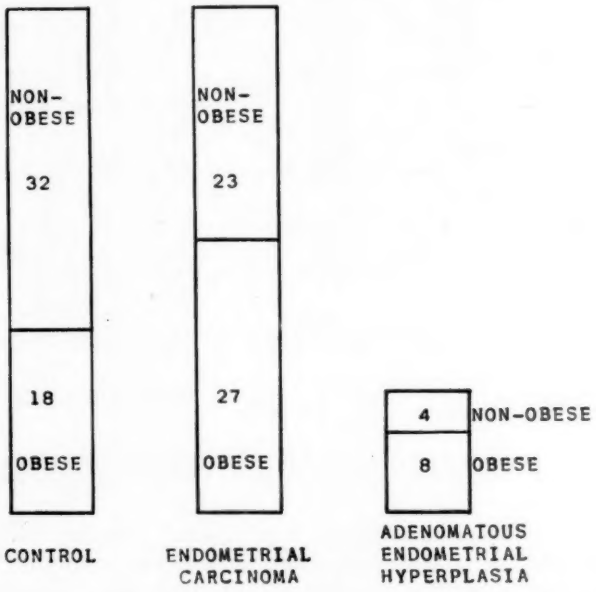

Fig. 3.—Comparison of the number of patients in each group who were classified as obese because their body weight was 160 pounds or more.

Obesity.—Fig. 3 shows the number of patients in each group who were considered obese because their body weight was 160 pounds or more. In the control group of patients, approximately one third were classified as obese, while more than one half of the endometrial carcinoma group were obese. The incidence of obesity was even greater in the patients with atypical endometrial hyperplasia. In this smaller group two thirds of the patients were considered obese.

Hypertension.—An evaluation of the incidence of hypertension in the three categories of patients is shown graphically in Fig. 4. Only one third of the control patients had blood pressure elevations above 140 mm. Hg systolic and 90 mm. Hg diastolic, while more than one half of the patients with endometrial carcinoma had concomitant hypertension. In the endometrial hyperplasia group approximately one half were hypertensive.

Parity.—A comparison of the parity of patients in the three groups, as shown in Fig. 5, indicates that nulliparity is about twice as frequent in patients with endometrial carcinoma as it is in those with no endometrial malignancy. The incidence of nulliparity in the patients with endometrial hyperplasia, however, is only slightly higher than in the control group.

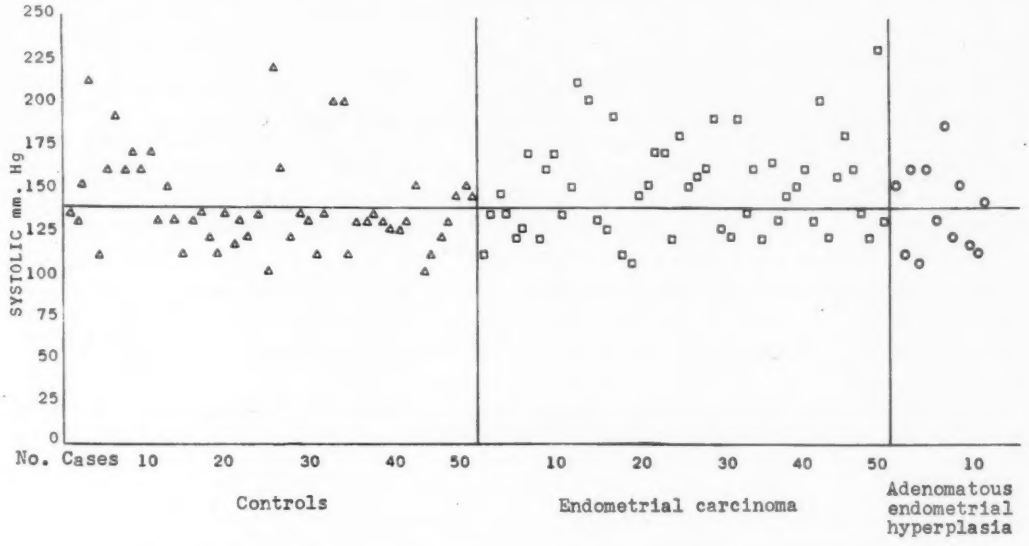

Fig. 4.—Incidence of hypertension in the three categories of patients.

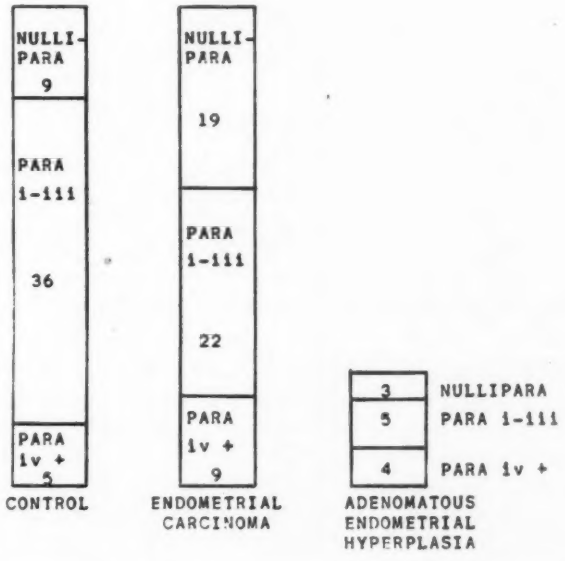

Fig. 5.—Distribution of patients according to parity in the three series.

Age at Menopause.—The occurrence of a high incidence of delayed menopause in patients with endometrial carcinoma was not noted in this study. Fig. 6 indicates that about one fifth of both the control patients and the patients with endometrial carcinoma experienced the menopause after 50 years of age.

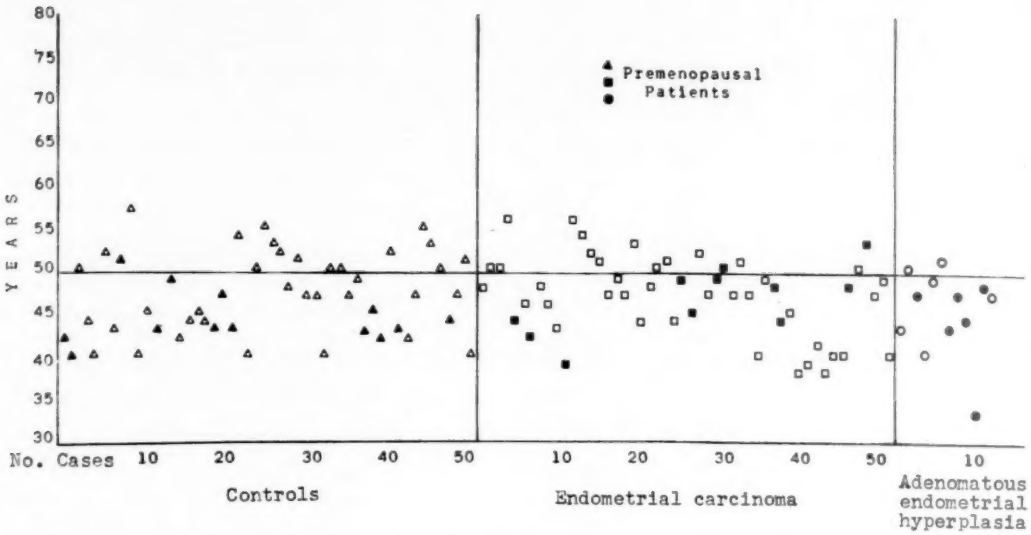

Fig. 6.—Distribution of patients according to age at the time of the menopause in the three categories.

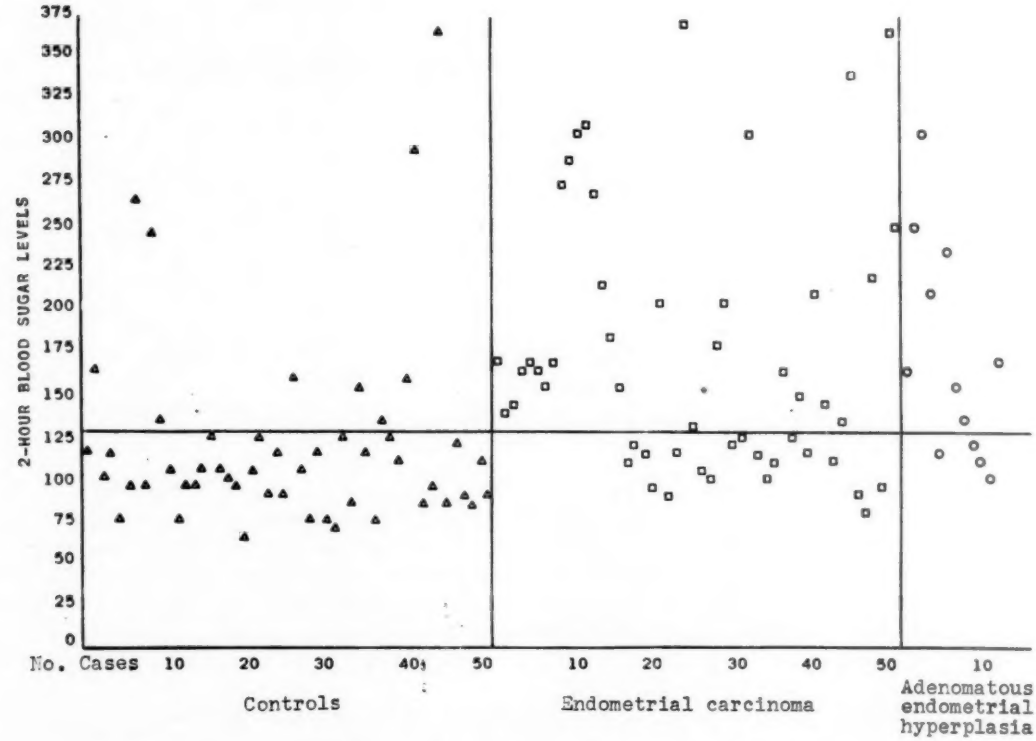

Fig. 7.—Distribution of patients according to the type of glucose tolerance curve in the control series and in the groups with endometrial carcinoma and adenomatous endometrial hyperplasia.

Patients in both categories experienced the menopause most commonly between the ages of 45 and 50 years. The number of patients in these groups who were premenopausal at the time of this evaluation were about equal.

Only 2 of the patients with adenomatous hyperplasia of the endometrium were more than 50 years of age when the menopause occurred. The remainder were all in the younger age groups, and the majority of these were premenopausal when the diagnosis was made.

Glucose Tolerance.—It is noted in Fig. 7 that in the control group of 50 patients approximately one fifth demonstrated a diabetic type of glucose tolerance curve. The glucose tolerance curves in the remaining four fifths of the patients without endometrial carcinoma were normal. Of these 10 patients with an abnormal glucose tolerance, 4 can be classified as having unquestionable diabetes, while the other 6 cases were of a questionable or mild type.

In the group of 50 patients with proved endometrial carcinoma, approximately two thirds had a diabetic type of glucose tolerance curve. One half of these patients can be considered to have a severe degree of abnormal glucose tolerance and unquestionable diabetes. The remaining one half of the group had curves indicative of mild or questionable diabetes. A comparison of the control group and the endometrial carcinoma group indicates that unquestionable diabetes is three times as common in the patients with endometrial carcinoma as in those without this lesion. Likewise, a reduced degree of glucose tolerance or mild diabetes is about twice as frequent in the patients with endometrial carcinoma as in those without this disease.

Of the 12 patients with adenomatous hyperplasia, two thirds had a diabetic type of glucose tolerance curve. This is comparable to the group in which unequivocal malignancy was present.

Comment

Corscaden,[10] in his discussion of the diagnostic factors encountered in patients with endometrial carcinoma, stated: "The picture of a more or less well-to-do woman, unmarried or if married childless, or at best with only one child, overweight, of a broad, husky habitus, with some degree of diabetes and hypertension, who has suffered in the past from excessive menstruation, suggests some constitutional abnormality in which the endocrine system may be regarded with suspicion if not with knowledge." The results of this clinical study, in which as many factors as possible were controlled, indicate that such constitutional abnormalities might well be regarded with concern when both the etiological and diagnostic problems associated with carcinoma of the endometrium are considered.

In this study the age at which the diagnosis of endometrial carcinoma was made coincides with the findings of most other reports. The diagnosis was determined in 70 per cent of these cases when the patients were 50 years of age or older. The peak incidence of 48 per cent occurred during the sixth decade, but 30 per cent of the patients were under 50 years of age when the cancer was initially discovered.

The frequent concurrence of obesity and endometrial carcinoma is well known. Tannenbaum[11] was of the impression that such a relationship is probably not a direct one, but that factors controlling weight are of more direct significance than weight itself. Young,[12] using a purified extract of the anterior pituitary growth hormone in adult dogs, produced an initial rise in body weight followed by the development of diabetes. Such a common factor of prolonged and excessive secretion of these diabetogenic growth-producing hormones of the anterior pituitary gland might well come into play as a cause

for the obesity which so frequently accompanies endometrial carcinoma in the human. The increased incidence of hypertension in patients with endometrial carcinoma is probably secondary to the obesity and lateral body build of these patients.

The diabetic tendency so frequently referred to in studies of endometrial carcinoma was confirmed in this series. Sixty-two per cent of the patients with endometrial carcinoma gave evidence of faulty glucose tolerance as compared to 20 per cent in the patients of the control group. Of the patients with endometrial carcinoma and associated abnormal glucose tolerance, 30 per cent were classified as having unquestionable diabetes. It appears that these findings might add further evidence to the hypothesis of prolonged and excessive secretion of the diabetogenic growth hormones of the anterior pituitary gland.

The occurrence of a delayed menopause in patients who developed endometrial carcinoma was not noted in this survey. Only 15 patients in this group experienced the menopause after 50 years of age. There were, however, 6 patients who were under 50 years of age and premenopausal at the time the diagnosis of carcinoma was made. There were also 4 patients under 50 years of age in whom the menopause had been induced by radiation therapy for benign causes, who later developed carcinoma of the endometrium. If these patients could be included as possibly experiencing the menopause after 50 years of age, the incidence would become 50 per cent. This figure is still somewhat below the 60 per cent incidence of late menopause cited by Crossen and Hobbs.[13] A possible explanation for this variation might be the confusion which may occur in the differentiation between true menstrual bleeding and bleeding from endometrial hyperplasia or carcinoma following shortly after the menopause.

The history of nulliparity and irregular bleeding at the time of, or after, the menopause was a feature commonly noted in the patients with endometrial carcinoma. Such evidence of excessive estrogen stimulation with resultant endometrial hyperplasia and polyp formation could well be incidental to the prolonged and abnormal secretion of the follicle-stimulating hormone by the anterior pituitary gland.

Hertig and Sommers, in their studies on the genesis of endometrial carcinoma, noted that adenomatous hyperplasia of the endometrium was frequently found 3 to 5 years preceding the development of carcinoma. Hertig also stated that, of the various processes preceding endometrial carcinoma, adenomatous hyperplasia was both most often observed, and found to show the most definite trend to increasing incidence as cancer approached. Numerous investigators[7, 14, 15] have pointed out the frequent association of adenomatous hyperplasia and adenocarcinoma in the endometrium of the same uterus. There are others[16, 17] who have gained the impression that adenomatous hyperplasia and anaplasia of the endometrium are irreversible conditions. In this study the similarity of the constitutional types in the patients with endometrial carcinoma and the smaller group with adenomatous hyperplasia, though statistically not significant, is suggestive of a common metabolic disorder as an etiological factor.

Conclusions

1. The constitutional factors of obesity, hypertension, nulliparity, irregular uterine bleeding at the time of the menopause, and faulty glucose tolerance occur with sufficient frequency in patients with endometrial carcinoma to be of diagnostic significance.

2. The same symptom complex is noted in a smaller group of patients with adenomatous hyperplasia of the endometrium. This is suggestive of a common metabolic disorder in patients with endometrial carcinoma and those with adenomatous hyperplasia.

3. There appears to be some evidence to suggest that prolonged overactivity of the anterior pituitary gland may lead to these diverse constitutional manifestations in both groups of patients.

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807 SPRUCE STREET

EARLY POSTRADIATION SURGERY FOR ENDOMETRIAL CARCINOMA*

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THERE appears to be general agreement among gynecologists that therapy which combines the advantages of surgery and irradiation offers the best chance of cure for the majority of patients with carcinoma of the uterine corpus. Two methods of delivering radiation share preference. Many prefer deep x-ray therapy postoperatively; others utilize intracavitary radium prior to operation. At Bellevue Hospital the preferred method of therapy for many years has been a single preoperative application of radium. The dosage usually has been 6,000 to 8,000 mg. hr. and has been followed by total abdominal hysterectomy and bilateral salpingo-oophorectomy after approximately 6 weeks. This plan of therapy is not peculiar to Bellevue Hospital.

It has become apparent that the use of radium in this fashion has one primary objective—the destruction of superficial carcinoma so that its dislodgment during surgical manipulation will not result in implantation of tumor at the various exposed operative sites.[2, 3] Examination of removed uteri frequently shows that there has been little or no radiation effect on tumor which has grown deep into the myometrium or lies a considerable distance from the source of radiation, as for example in the adnexa. We have observed instances where there was unmistakable evidence of rapid growth of extrauterine carcinoma during the 6 week period between the application of radium and hysterectomy. A patient with a freely movable uterus and no adnexal masses, following removal of the radium, was found to have limited uterine mobility and palpable adnexal masses when she returned for hysterectomy 6 weeks later. Extensive extrauterine carcinoma was found at operation. It was this observation that prompted the present study. It is doubtful that there is often a radiation effect on lymph nodes involved by carcinoma.

In the absence of a consistent radiation effect on all tumor tissue within the pelvis, there appear to be certain disadvantages in delaying hysterectomy for a period of 6 weeks after the application of radium. Tumors with a rapid growth potential should be capable of considerable advancement during this interval if they have not been inhibited by radiation. One of the principal objections to the use of preoperative intracavitary radium, expressed by

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several authors in the recent literature, is based on this long period of delay after the diagnosis has been made and definitive therapy has been accomplished.[1, 3, 5]

Radiologists indicate that after 6 weeks tumor tissue has undergone the maximum effect of radiation. If the tumor is spilled or left unremoved it does not seem conceivable that the radiation effect will cease because surgery has been undertaken prior to the conclusion of this arbitrary period.

Gynecologists have indicated that an acute radiation effect takes place shortly after the application of radium and will make the operation technically difficult. This effect, consisting of congestion and edema, is said to subside in approximately 6 weeks and operation can then be performed with less difficulty.

An infected uterine discharge which often accompanies endometrial carcinoma will be eliminated by intracavitary radium but this requires some weeks.[6] Although of extreme importance in another era of surgery, peritonitis is not now a primary threat in the management of endometrial carcinoma.

Material and Method

On the basis of some of these premises and to test the validity of others, a variation in the usual pattern of therapy has been undertaken. Since 1953, 14 patients with carcinoma of the endometrium have received intracavitary radium followed by hysterectomy 3 to 19 days after the removal of the radium. The radium was introduced in the form of a tandem with as many single applicators as could be conveniently inserted in the uterine cavity in order to obtain a uniform radiation effect on the entire surface of the tumor. The total amount therefore varied depending on the capacity of the cavity, but ranged between 4,000 and 8,280 mg. hr.

Surgical Observations

There have been too few cases and insufficient time has elapsed to permit a complete evaluation of this form of treatment. Certain observations do appear to be valid and significant, however. Most obvious of these is the facility with which the hysterectomy can be performed. Technically the operations were made no more difficult when undertaken so shortly after radium therapy. Occasionally there appeared to be some increased vascularity of the tissues in the operative field but this was no more than the annoying ooze frequently encountered in the nonirradiated patient. Blood loss was not a major problem and the incidence of blood transfusion was no greater than that in patients undergoing hysterectomy for nonmalignant diseases.

Slight edema of tissues was sometimes noted, particularly in the broad ligaments and beneath the bladder reflection of the peritoneum, but this was not an obstacle to an efficient operative procedure. In fact, edema in these areas occasionally made the delineation of tissue planes more clear, for easier dissection.

Healing of tissue has been unaltered and primary union of the abdominal wound has been the rule. The single exception was the dehiscence of an abdominal wound in an extremely obese patient, which healed after secondary closure.

Histological Observations

Of paramount importance, however, was the effect of radiation on the tumor (Table I). In the 14 cases studied, residual tumor could be found in 7 instances. There was evidence of a definite radiation effect in all of these, although the tumor had not been completely obliterated. These uteri were removed 3 to 17 days after the radium. In one of these, tumor was present in the ovary but was not found in the uterus. In the instances where tumor remained in the endometrium there was consistently an area of superficial necrosis lining the surface but it was impossible to determine whether this was intact throughout the cavity (Figs. 1 and 2). These patients received 4,000 to 8,280 mg. hr. of therapy with a single application.

TABLE I. PATIENTS TREATED BY EARLY POSTRADIATION SURGERY

PATIENT	DATE	AGE	SIZE OF UTERUS (INCHES)	RADIUM DOSE (MG. HR.)	INTERVAL (DAYS)	RESIDUAL TUMOR	FOLLOW-UP
M. R.	12/54	72	3½	6,720	3	Uterus	No follow-up
C. C.	4/55	62	5	8,280	13	Cervix	18 months, no recurrence
H. H.	6/54	69	4	7,735	12	Uterus	2½ years, no recurrence
S. C.	8/53	47	3	7,630	14	Uterus Ovary	6 months, no recurrence
C. S.	12/53	55	4	7,905	12	Uterus	6 months, no recurrence
L. V.	2/54	62	3	7,920	13	Uterus	No follow-up
A. S.	2/54	61	2½	4,000	12	Uterus	3 years, no recurrence
R. C.	12/54	34	2¾	8,160	5	None	No follow-up
H. A.	3/56	67	2¾	6,000	19	None	Died. Gastrointestinal hemorrhage
V. O.	8/55	67	4	7,680	19	None	1 year, no recurrence
M. M.	1/53	58	3½	6,720	16	None	2 years, no recurrence
R. G.	12/54	31	3	8,000	5	None	2 years, no recurrence
G. C.	4/54	73	2	7,820	11	None	2 years, no recurrence
M. C.	4/54	67	2	4,100	11	None	3 years, no recurrence

In the remaining 7 cases, no tumor could be found in the removed uterus or adnexa (Fig. 3). These hysterectomies were performed 5 days (2 cases) to 19 days (2 cases) after removal of the radium. These patients received 6,000 to 8,100 mg. hr. of radium in a single application.

Comment

Most authors report that radium destroys endometrial carcinoma in about 50 per cent of cases. This series, though small, compares favorably in this respect. More important, in accomplishing this end the delay in the removal of the uterus, which is cited by so many as an objection to the combined form of therapy, is reduced to a minimum.

Meigs[7] has employed this method of therapy but detailed results have not been published. Addington and Betts[8] have reviewed 20 cases in which 5,000 to 5,500 mg. hr. of radium was used and hysterectomy was performed within 24 to 36 hours after removal of the radium. The operation was made no more

difficult. Unfortunately, they did not indicate what radiation effect, if any, had occurred after this short period of time. Fourteen of these patients were apparently well up to 2 years after removal of the tumor.

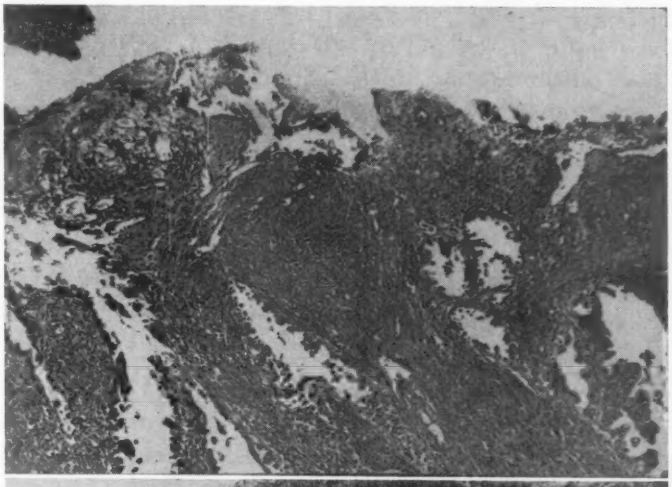

Fig. 1.

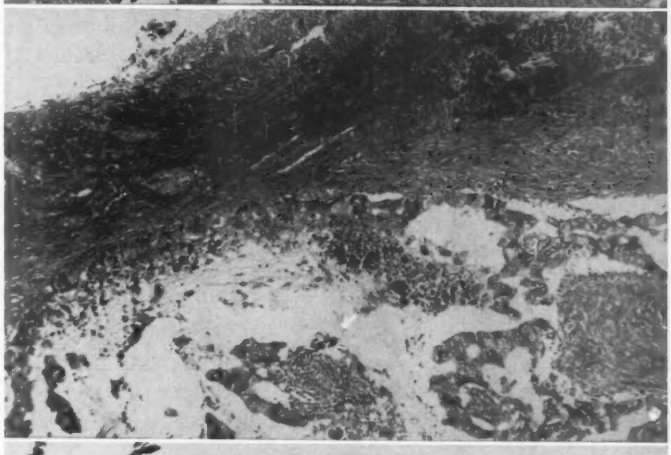

Fig. 2.

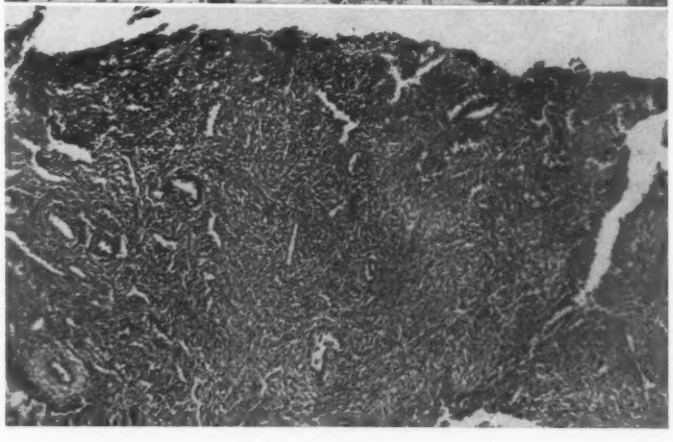

Fig. 3.

Fig. 1.—M. R. Endometrium 3 days after 6,720 mg. hr. of radium showing radiation effect on superficial tumor.

Fig. 2.—A. S. Endometrium 12 days after 4,000 mg. hr. of radium showing tumor with marked radiation effect.

Fig. 3.—R. C. Endometrium 5 days after 8,160 mg. hr. of radium showing complete necrosis of tumor.

Although the present series is small and the elapsed time since therapy is short, it is interesting to note that none of the 10 patients followed has shown evidence of persistent or recurrent tumor. This follow-up period ranges from 6 months to 3 years. Three patients failed to return for follow-up.

There was one death in this series. This resulted from massive hemorrhage from nonspecific ulceration of the esophagus and did not appear to be related to the radium therapy or to the surgery.

Conclusions

On the basis of 14 cases reported here it appears possible and perhaps desirable to reduce the conventional waiting period between the application of radium and the surgical removal of the uterus in patients with carcinoma of the endometrium. Although the period of delay varies considerably in this series one gains the impression that the results would be similar if this period were reduced to from 7 to 10 days.

There is some doubt that the upper limits of dosage utilized in this series are necessary. Probably the 4,000 to 6,000 mg. hr. range would suffice for the purpose intended, namely, the destruction of superficial tumor tissue.

Follow-up to date indicates excellent results in this small series, but no conclusion should be drawn as yet.

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STUDIES IN HUMAN REPRODUCTION

II. The Influence of Diabetes Mellitus in Men Upon Reproduction

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IT IS well recognized that diabetes mellitus may have an unfavorable influence upon a woman's reproductive capacity, as exemplified by an increased incidence of abortions, stillbirths, intrapartum and neonatal deaths, and excessive-sized fetuses.[1] Little has been written concerning the influence of diabetes mellitus on the reproductive capacity of men. The scant data include Jackson's[2] recent report that infants of diabetic fathers are significantly heavier at birth than infants of nondiabetic men. The other scattered reports deal with an occasionally decreased 17-ketosteroid excretion in diabetic men,[3] infrequent atrophy of the testicles,[4] uncommon calcification of the vas deferens,[5] and an impression of an increased incidence of impotence.

In the present investigation, 198 diabetic men were studied in relation to their reproductive histories. Preliminary data have been presented elsewhere.[6, 7]

Material and Methods

One hundred ninety-eight unselected men attending the Outpatient Diabetes Clinics of the Hospital of the University of Pennsylvania and the Philadelphia General Hospital served as subjects. Their ages at the onset of diabetes ranged from 2½ to 78 years. One hundred sixty-eight were, or had been, married. Men whose wives were known to have diabetes were excluded from the study.

The subjects' medical records were examined and abstracted. Each subject was questioned regarding his general health, reproductive history, and sex habits. If married, his age at marriage, use of contraception, number of pregnancies engendered, their clinical course and outcome, age and health of the spouse, and so on, were ascertained.

Controls were obtained by similarly interviewing 168 married men attending the Outpatient Clinics of the Dental School of the University of Pennsylvania. Questions concerning sex habits were omitted. Individuals who were known to have diabetes, or whose wives had diabetes, were excluded.

Results

Incidence of Impotence.—Impotence occurred at an earlier age and more frequently among the 198 diabetic men than it did among the 4,108 men studied by Kinsey and his associates.[8] As shown in Table I, from the age of 30 to 34 years on, the *cumulative incidence* of impotence in the diabetic men was two

to five times as high as in the population studied by Kinsey. This difference is statistically significant from the 35 to 39 year age group through the 65 to 69 year age group.* The *incidence* of impotence *by 5 year age groups* (Table II) gradually increased from 25 per cent in the 30 to 34 year age group to almost 75 per cent in those 60 to 64 years of age.

TABLE I. CUMULATIVE INCIDENCE OF IMPOTENCE IN 198 DIABETIC MEN, COMPARED WITH ITS INCIDENCE AS REPORTED BY KINSEY AND ASSOCIATES[8]

AGE (YEARS)	POPULATION		NO. IMPOTENT		% IMPOTENT	
	DIABETIC	KINSEY	DIABETIC	KINSEY	DIABETIC	KINSEY
10-14	198	4,108	0	0	0.00	0.00
15-19	198	3,948	0	2	0.00	0.05
20-24	196	3,017	1	3	0.51	0.10
25-29	190	1,627	0	6	0.00	0.37
30-34	186	1,025	5	8	2.68	0.80
35-39	182	741	9	10	4.91*	1.30
40-44	174	513	13	10	7.46*	1.90
45-49	158	347	21	9	13.30*	2.60
50-54	145	236	34	16	23.20*	6.70
55-59	117	134	31	9	26.40*	6.70
60-64	87	87	35	16	40.20*	18.40
65-69	63	44	36	11	57.10*	25.00
70-74	36	26	21	7	58.40	27.00
75-79	15	11	11	5	73.40	45.40
80-84	5	4	4	3	80.00	75.00
85-89	1	—	0	—	0.00	—
90-94	1	—	0	—	0.00	—

*Statistically significantly higher than Kinsey's population (chi square analysis, P = < .01).

TABLE II. INCIDENCE OF IMPOTENCE BY AGE AMONG 198 DIABETIC MEN

AGE (YEARS)	NUMBER OF SUBJECTS	% IMPOTENT
15-19	2	0.0
20-24	6	16.7
25-29	4	0.0
30-34	4	25.0
35-39	8	25.0
40-44	16	37.5
45-49	13	38.5
50-54	28	53.6
55-59	30	66.7
60-64	23	73.9
65-69	28	67.9
70-74	21	57.1
75-79	10	70.0
80-84	4	100.0
85-90	1	0.0

Duration of Diabetes and Incidence of Impotence.—Seventy per cent of the men with diabetes of less than one year's duration suffered from impotence. Among those who had had diabetes for one to 5 years, the incidence dropped to 43 per cent. It was 45 per cent among those who had had diabetes for more than 5 years. Thus, the incidence of impotence did not increase with the greater duration of the disease. The fact that 70 per cent of the men with a recent onset of diabetes (less than one year) were impotent may have been due to the fact that many of them had just been found to be diabetic, and hence the disease often had not yet been well controlled. It was not uncommon for patients to report that until the diabetes had been stabilized, they had been impotent, with a return of potency when the diabetic state was controlled. In

*Chi square analysis. P = < .01.

the cases in which impotence occurred while the diabetes was well controlled, however, it usually was more or less permanent. The generally high incidence of impotence probably is related to the fact that most of the men were in the older age groups.

Actually, 30 per cent of all those who became impotent did so within one year of the clinical recognition of diabetes. Sixty per cent of the men who subsequently developed impotence did so within 5 years of the onset of diabetes.

Severity and Complications of Diabetes and Impotence.—The incidence of impotence was apparently not related to the severity of the diabetes, when the latter was graded according to carbohydrate tolerance and insulin requirement, as outlined by Wilder.[9] However, poor control of the diabetes, with episodes of acidosis or hypoglycemia, often was associated with transient periods of impotence. Complications of diabetes, such as peripheral vascular disease, neuropathies, retinopathies, renal or cardiovascular disease, were no more frequent among the impotent diabetics than among those who were potent.

Impotence and "Preclinical" Diabetes.—There was no higher incidence of impotence among the diabetic men prior to the clinical onset of diabetes than was reported by Kinsey and associates[8] for their population.

TABLE III. COMPARISON OF FERTILITY OF DIABETIC AND NONDIABETIC MEN

CHARACTERISTICS	WIVES OF DIABETIC MEN		WIVES OF NONDIABETIC MEN	
	NO.	%	NO.	%
Population	168		168	
Total conceptions	555		390	
Conceptions per family	3.3		2.3	
Conceptions per year of exposure*	0.221		0.215	
Abortions†	92	16.6‡	40	10.0
Premature births§	22	4.8	22	6.3
Stillbirths	12	2.6	11	3.1
Twins	5		4	
Term births	441	95.2	328	93.7
Male	237	54	163	49.7
Female	204	46	165	50.3
Sterility‖	28	18.3	24	15.3

*Years of cohabitation without contraception prior to the age of 45 for the husband and 40 for the wife.

†Termination of pregnancy prior to the twenty-eighth week.

‡Significantly different from nondiabetic group (chi square = 7.10, $P < .01$).

§Termination of pregnancy between the twenty-eighth and the thirty-seventh week or birth weight less than 5½ pounds.

‖Cohabitation without contraception for at least 2 years by the age of 45 for the husband and 40 for the wife without conception.

Fertility.—One hundred and sixty-eight of the diabetic men were or had been married. The diabetic group averaged 3.3 conceptions each, compared with 2.3 for the control population (Table III). This difference is not statistically significant. In each group there were individuals who had married too late in life to reproduce, or who were so young that they might not have completed their reproductive careers. Therefore, in order to compare more accurately the fertility data for the two groups, the actual number of years of exposure to the possibility of conception was calculated for each group. This was done by determining for each couple the number of years of cohabitation without contraception prior to the age of 45 for the husband and age 40 for the wife. The average number of conceptions per year of exposure was found to be 0.221 for the diabetic men and 0.215 for the control series. This difference is not statistically significant (t test).

Fertility and "Preclinical" Diabetes.—The diabetic population included many individuals who did not have diabetes during their reproductive years. In an attempt to ascertain whether there was any difference in fertility during the diabetic state as compared with the "prediabetic" state, the 22 married men known to be diabetic before the age of 45 were studied. This group averaged 0.250 conceptions per year of exposure, a figure comparable both to that cited above for the entire diabetic population and to that of the control group.

Sterility.—This was defined as at least 2 years of cohabitation without contraception prior to the age of 45 for the husband and 40 for the wife without conception.

There was no statistical difference in the incidence of sterility among the diabetic individuals compared with the control population. Eighteen and three-tenths per cent of the wives of the diabetic men had no conceptions, compared with 15.3 per cent of the wives of the control population.

Incidence of Abortion (Termination of Pregnancy Prior to the Twenty-eighth Week of Gestation).—The wives of the diabetic men had a significantly higher incidence of abortions (chi square = 7.10, $P < .01$), compared with the control population (Table III). Sixteen and six-tenths per cent of the 555 conceptions of the wives of the diabetic men ended in abortions, compared with 10.0 per cent of the 390 conceptions among the wives of the controls. In an attempt to clarify this finding, the diabetic and control populations were compared for factors which might influence the incidence of abortion, such as age of husband and wife at the time of conception, and race. The ages of both male and female at marriage did not differ significantly between the diabetic and control populations. There was no significant difference in the incidence of abortion between white and Negro diabetics ($\chi^2 = 0.43$). The incidence of abortion in white diabetic individuals was significantly higher than in the white controls ($\chi^2 = 6.74$, $P < .01$), but was not significantly different for Negro diabetic versus Negro control ($\chi^2 = 3.17$, $P < .10 > .05$). The incidence of abortion before and after the clinical recognition of the diabetes did not differ significantly.

Birth Weights of Offspring.—No significant differences were found between the average birth weights of the children of diabetic fathers and those of the control fathers (chi square analysis) (Table IV). The weights of the offspring of the diabetic men also closely approximated birth weight data for the United States as given in the most recent summary of the Office of Vital Statistics.[10] The latter report, it should be pointed out, is compiled from birth certificates and uses a slightly different weight classification.

TABLE IV. COMPARISON OF BIRTH WEIGHTS OF OFFSPRING OF DIABETIC AND NONDIABETIC MEN

POPULATION	NO. CHILDREN	DISTRIBUTION OF CHILDREN BY WEIGHT*			
		UNDER 8 POUNDS (%)	8-8.9 POUNDS (%)	9-10 POUNDS (%)	OVER 10 POUNDS (%)
Diabetic	274	67.9	17.5	8.4	6.2
Nondiabetic	279	71.0	18.6	6.2	4.3
United States, 1951†	3,000,000	66.0	26.0	7.0	2.0
United States Weight Criteria		(Less than 7 pounds, 12 ounces)	(7 pounds, 12 ounces to 8 pounds, 13 ounces)	(8 pounds, 14 ounces to 9 pounds, 14 ounces)	(9 pounds, 15 ounces and over)

*Jackson's weight classification.[2]
†U. S. Department of Health, Education and Welfare.[10]

Premature Births, Stillbirths, Malformations, and Sex of Offspring.—The incidence of premature births, stillbirths, and malformations, and the sex ratio of the offspring did not differ significantly from those of the control population.

Summary

One hundred and ninety-eight men attending outpatient diabetes clinics were interviewed with respect to their reproductive histories. Twenty-five per cent of the subjects 30 to 34 years of age were impotent. The incidence gradually increased with age so that by 50 to 54 years, 53.6 per cent were impotent. The incidence of impotence was apparently not related to the age at onset of the diabetes, its duration or severity, or the presence of vascular or neurological complications.

The diabetic men reported a significantly higher incidence of abortions among their wives than did a control population obtained at random from among nondiabetic men attending an outpatient dental clinic. The diabetic group exhibited no significant differences from the controls with respect to the incidence of conceptions, premature births, stillbirths, malformations, sex ratio of the offspring, and birth weights of offspring.

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FOLLICULAR AND TUBAL FLUIDS IN THE REPRODUCTIVE PROCESS*

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THE studies of Farris and Fornwalt[1] indicate that human ovarian follicular fluid and tubal (hydrosalpinx) fluid can increase the speed of spermatozoa. Kurzrok and associates[2] reported that human follicular fluid prolongs the life span of human sperm. If these fluids actually are beneficial to spermatozoa, perhaps they play a greater role in the reproductive process than hitherto has been recognized. Therefore further studies seemed indicated. The purpose of this study was to test the effect of the body fluids that might be associated with the reproductive process, such as follicular fluid, tubal (hydrosalpinx) fluid, and peritoneal fluid, upon sperm motility, count, and longevity.

Methods and Materials

Human follicular fluid, other ovarian cyst fluid, hydrosalpinx and peritoneal fluids were obtained at operations performed at The Graduate Hospital, University of Pennsylvania. They were aspirated with a sterile needle and syringe, transferred to sterile containers, and transported to The Wistar Institute for processing and testing. Six different types of body fluids were obtained from 25 patients, as follows: follicle cyst, 8; hydrosalpinx, 4; peritoneal, 2; pseudomucinous cyst, 3; corpus luteum cyst, 4; parovarian cyst, 4.

A histologic diagnosis of all of the ovarian cysts and inflamed Fallopian tubes was made by tissue examination in the pathology laboratory of The Graduate Hospital. Each specimen was cultured in order to rule out possible contamination. Even though all of the fluids were found to be sterile, they were passed through a Seitz filter as an added precaution. This filtration did not affect the behavior of the fluid on spermatozoa.

All fluids were tested for their effect upon sperm drive in vitro. An attempt was made to test each fluid upon the semen from 3 men within the same fertility classification. The semen samples were obtained from donors at The Wistar Institute. The specimens were examined within 30 minutes to 1 hour after emission. The fertility classification followed was that suggested by Farris[3] (based on total ejaculate): highly fertile, 185 million motile cells or more; relatively fertile, 80 million to 185 million motile cells; subfertile, less than 80 million motile cells.

The main purpose was to study the effect of these fluids on the speed of the sperm. Additional studies were performed to test their effect upon sperm

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count and longevity. Specimens that were found to increase sperm drive were stored in a freezer for future use.

Method of Sperm Counting.—For the exact method of sperm counting, the reader is referred to Farris's book.[3] In brief, the spermatozoa count was made like a blood count, with the use of an ordinary white-cell pipette (1:20 dilution) in the red-cell field of a Spencer Bright-Line hemacytometer. Locke's fluid was used as a diluent for the control semen count.

Both compartments of the counting chamber were used, the upper compartment to study the effect of the control fluid, and the lower to study the effect of the experimental fluid on the same semen sample. The counting and timing of the sperm were done promptly after dilution. The difference between the sperm count with the control fluid (Locke's fluid) and the count with the experimental fluid revealed the effect of the experimental fluids on the live sperm count.

Method of Measuring Speed (Drive) of Sperm.—The speeds of 5 spermatozoa were studied in each of the 5 blocks (25 cells in all). For details of counting, see Farris's[3] text. The difference in time between the average speed of the control sample and the average speed of the same semen sample with the experimental fluid used as a diluent, revealed the effectiveness of the experimental fluid. According to the work of Farris, rapidly progressive sperm cross the square in 1 second or less; progressive spermatozoa cover the same distance in from 1.0 to 1.9 seconds; sluggish spermatozoa require 2 seconds or more to cross the 0.05 mm. square.

Method of Measuring Life Span (Longevity) of Sperm.—Sperm longevity studies were performed with fluids from a limited number of follicle cysts and hydrosalpinges. Two methods were used in measuring longevity:

1. Hanging-drop method: Two drops of semen were added to 2 drops of the experimental fluid on a cover glass and inverted over a hanging-drop slide. The margin of the cover glass was rimmed with a lubricating jelly to prevent drying. This preparation was kept at room temperature and observed for gross activity at planned intervals. A control preparation prepared with Locke's fluid was similarly observed.

2. Syringe method: One-tenth cubic centimeter of semen was added to 0.1 c.c. of the experimental fluid in a tuberculin syringe. The tip of the syringe was stoppered by means of a sterile metal cap, and this preparation was allowed to remain at room temperature. A control was prepared with Locke's fluid. Specific amounts of each preparation were removed at regular intervals. They were examined for the number of living sperm per cubic centimeter and the speed of drive, with the use of the hemacytometer.

Results

1. The Effect of Body Fluids Upon Sperm Drive.—

A. Follicle-cyst fluid: A semen specimen from each of 10 different men classified as *highly fertile* was obtained for this study (Table I). It was noted that when follicle-cyst fluid was used as a diluent for the semen of these 10 highly fertile men, the speed of sperm was increased in all specimens.

A semen specimen from each of 17 different men classified as *relatively fertile* was used in a second series of studies (Table I). Sixteen showed an acceleration of sperm travel.

A semen specimen from each of 10 different men classified as *subfertile* was used for a third series of observations. Eight showed an acceleration of sperm travel. Five of these specimens were improved from a sluggish to a progressive type of motility.

TABLE I. THE EFFECT OF BODY FLUIDS ON SPERM DRIVE

BODY FLUID		DONOR SEMEN SAMPLE		EFFECT OF ADDITION OF EACH BODY FLUID TO DONOR SEMEN SAMPLES				
				NO. OF SAMPLES IN WHICH SPERMATOZOA WERE ACCELERATED	RANGE OF ACCELERATION OF SPERM DRIVE. NO. OF SECONDS LESS TIME THAN CONTROL SPEED TO TRAVEL 0.05 MM.	NUMBER OF DONOR SAMPLES ACCELERATED		
TYPE	NO. OF DIFFERENT SPECIMENS	FERTILITY CLASSIFICATION	NO. OF DIFFERENT DONORS			0.5 SECOND OR MORE	0.2 TO 0.5 SECOND	LESS THAN 0.2 SECOND
Follicle cyst	8	Highly fertile	10	10	0.1-0.5	0	8	2
		Relatively fertile	17	16	0.1-0.4	0	11	5
		Subfertile	10	8	0.1-1.6	5	2	1
Hydrosalpinx	4	Highly fertile	9	9	0.2-0.5	0	9	0
		Relatively fertile	16	14	0.1-0.5	0	10	4
		Subfertile	8	6	0.1-0.7	2	3	1
Peritoneal	2	Highly fertile	5	5	0.3-0.4	0	5	0
		Relatively fertile	6	6	0.1-0.3	0	4	2
		Subfertile	1	1	1.7	1	0	0
Pseudomucinous cyst	3	Highly fertile	3	0	----	--	--	--
		Relatively fertile	3	1	0.3	0	1	0
		Subfertile	6	1	0.2	0	1	0
Parovarian cyst	4	Highly fertile	4	2	0.1-0.3	0	1	1
		Relatively fertile	8	4	0.2-0.5	0	4	0
		Subfertile	6	2	0.1-0.3	0	1	1
Corpus luteum cyst	4	Highly fertile	5	4	0.2-0.5	0	4	0
		Relatively fertile	5	2	0.4-0.5	0	2	0
		Subfertile	6	2	0.3-0.6	1	1	0

B. Hydrosalpinx fluid: A semen specimen from each of 9 different men classified as *highly fertile* was used for one part of this study. All specimens showed an acceleration of sperm travel.

A semen specimen from each of 16 different men classified as *relatively fertile* was included in this second series of observations. Fourteen of these specimens showed an acceleration of sperm drive.

A semen specimen from each of 8 different men classified as *subfertile* was employed for a third series. Six of these specimens showed an acceleration of sperm drive.

C. Peritoneal fluid: A semen specimen from each of 5 different donors classified as *highly fertile* was used for part of this study. All specimens showed an acceleration of sperm travel when this fluid was added as a diluent.

A semen specimen from each of 6 different men classified as *relatively fertile* formed the second group. All of the semen specimens showed an acceleration in sperm drive when this fluid was added as a diluent.

One *subfertile* donor was obtained for study with use of peritoneal fluid. A marked acceleration of sperm drive was noted.

D. Other fluids (pseudomucinous cyst, parovarian cyst, and corpus luteum cyst): These fluids were either harmful to or had no constant beneficial effect upon the sperm drive.

2. The Effect of Body Fluids on Sperm Drive and Number of Active Sperm.—The total number of active sperm was not increased significantly by the fluids which accelerated the drive of the sperm (Table II). The fluids which

improved sperm drive did not decrease the living count of the semen sample. Apparently the increase in speed of the individual spermatozoon does not occur at the expense of the living count; that is, gain in speed by one spermatozoon was not compensated for by death of many other spermatozoa. In the fluids that were harmful to sperm drive, it was often noted that the live count was reduced.

TABLE II. THE EFFECT OF BODY FLUIDS ON SPERM DRIVE AND NUMBER OF ACTIVE SPERM

BODY FLUID		DONOR SEMEN SAMPLE		EFFECT OF ADDITION OF EACH BODY FLUID TO DONOR SEMEN SAMPLES			
				NO. OF SAMPLES IN WHICH SPERMATOZOA WERE ACCELERATED	NO. OF DONOR SAMPLES IN WHICH NO. OF ACTIVE SPERMATOZOA WERE:		
TYPE	NO. OF DIFFERENT SPECIMENS	FERTILITY CLASSIFICATION	NO. OF DIFFERENT DONORS		UNCHANGED	INCREASED	DECREASED
Follicle cyst	3	Highly fertile	5	5	4	1	0
		Relatively fertile	5	5	5	0	0
		Subfertile	6	4	6	0	0
Hydrosalpinx	3	Highly fertile	5	5	5	0	0
		Relatively fertile	4	4	4	0	0
		Subfertile	5	3	5	0	0
Peritoneal	2	Highly fertile	3	3	3	0	0
		Relatively fertile	2	2	1	1	0
		Subfertile	1	1	1	0	0
Pseudomucinous cyst	2	Highly fertile	3	1	0	0	3
		Relatively fertile	3	0	0	0	3
		Subfertile	3	0	0	0	3
Corpus luteum cyst	2	Highly fertile	3	2	3	0	0
		Relatively fertile	3	1	3	0	0
		Subfertile	3	1	3	0	0

TABLE III. THE EFFECT OF BODY FLUIDS ON SPERM DRIVE, NUMBER OF ACTIVE SPERM, AND LONGEVITY OF SPERM

CONTROL SEMEN SAMPLE	EFFECT OF THE ADDITION OF EACH BODY FLUID TO THE DONOR SEMEN SAMPLE							DURATION OF EXPERIMENT
	FOLLICLE CYST (F) FLUID				HYDROSALPINX (T) FLUID			
	F 1	F 2	F 3	F 4	T 1	T 2	T 3	
Time to Travel 0.05 mm. (Seconds).—								
1.3	0.8	0.7	0.8	0.8	0.9	1.0	1.1	Start
1.5	1.0	1.1	1.0	0.9	1.1	1.0	1.1	4 hours later
1.9	0.9	1.3	1.4	1.0	1.2	1.1	1.3	6 hours later
No. of Active Sperm (Millions/c.c.).—								
23.0	24.5	24.0	23.0	23.5	23.5	23.0	24.0	Start
23.0	23.0	24.0	23.0	23.0	23.0	23.0	23.5	4 hours later
11.5	12.0	11.0	13.0	12.0	12.5	12.2	13.0	6 hours later

3. The Effect of Body Fluids on Sperm Drive, Number of Active Sperm, and Longevity of Sperm.—One donor sample was used with 4 different follicle cyst fluids and 3 different specimens of hydrosalpinx fluid. Each fluid was studied by two techniques, (a) hanging-drop technique (for gross activity) and (b) tuberculin syringe technique (for chamber counts) (Table III).

A. Hanging-drop method: In the control sample with Locke's fluid as a diluent (Fig. 1), sperm activity was detected for as long as 11 hours. In the follicle-cyst-fluid specimens, activity continued for as long as 24 to 30 hours.

Results with hydrosalpinx fluid (Fig. 2) were similar to the results with follicle-cyst fluid.

B. Syringe technique: Individual chamber counts and estimation of speed were possible up to the sixth hour only (Table III), because of the limited quantity of experimental fluid. In general it will be noted that the drop in sperm count with follicle-cyst and hydrosalpinx fluid diluents was practically identical with that of the control. The improved sperm drive (speed) with the experimental diluents persisted, however, as contrasted with a slowing up of the drive of the sperm in the control series. Thus, increase in speed of the sperm is produced with these fluids without harm to longevity or live count, at least within a 6 hour interval.

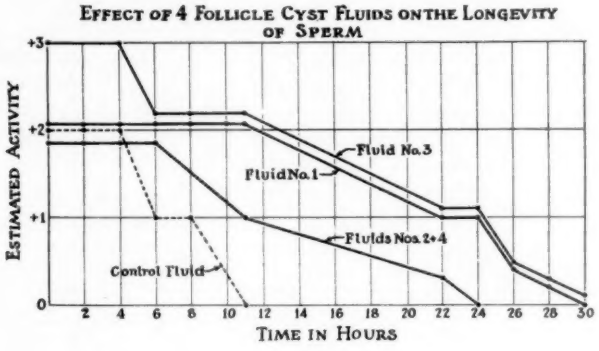

Fig. 1.

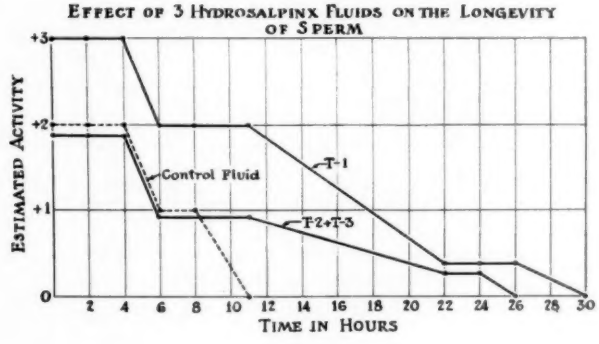

Fig. 2.

Comments

The in vitro studies reported upon in this paper indicate that human follicle-cyst fluid, hydrosalpinx fluid, and peritoneal fluid are beneficial to the semen sample. Other types of ovarian-cyst fluid were found to have little or no beneficial effect. The beneficial effect of follicle-cyst, hydrosalpinx, and peritoneal fluids was noted specifically upon the speed of the spermatozoa. The sperm drive was improved to about the same degree in all male fertility classes. This acceleration was accomplished without deleterious effect upon longevity or viability of the semen. The longevity of the semen was increased approximately 2 to 3 times (up to 30 hours) when follicle-cyst and hydrosalpinx fluids were added. This fell far short of the 96 hour life span reported by Kurzrok and associates,[2] however, with the addition of follicular fluid.

Method of Action of Fluids.—In seeking the modus operandi by which follicular fluid exerts its beneficial effect upon the semen, it has been ventured by previous investigators[2] that perhaps this fluid acts as an extracellular nutrient for human spermatozoa. Spermatozoa possess probably only a small intracellular reserve, and depend apparently for survival largely upon extracellular nutrients in the seminal fluid and secretions within the female genital tract. It may well be possible that the follicular fluid acts as such an extracellular nutrient. Human follicle-cyst fluid, tubal (hydrosalpinx) and peritoneal fluids may possess an "energizing" substance which increases the speed of the spermatozoa. Why hydrosalpinx and peritoneal fluids give effects similar to those of follicular fluid is yet unknown. From preliminary work upon the chemical nature of follicular fluid, follicle-cyst fluid, hydrosalpinx and peritoneal fluids, Perloff and co-workers[4] reported that all of these fluids may merely be exudates of blood serum from which certain proteins are specifically removed (particularly the alpha-2 fraction). Here may lie their common denominator.

It was interesting to note that hydrosalpinx fluid, which results from an inflammatory process, should benefit sperm drive and longevity. Weisman[5] has reported that pus and necrotic material also have no inhibitory effect on human sperm survival. In fact, he has shown that these materials may even prolong the motility of spermatozoa. It is, of course, also possible that hydrosalpinx fluid and normal tubal fluid, when analyzed, may prove to be chemically similar.

Possible Role of Follicular Fluid in the Process of Fertilization.—The information gained from these experiments with follicular fluid has given rise to the following question: Does follicular fluid play a more important part in the normal fertilization process than has hitherto been recognized? It may be that the ultimate role of follicular fluid in the physiologic reproductive mechanism is as follows: at about 2 days prior to midcycle,[3] the mature Graafian follicle ruptures, releasing the ovum bathed in its follicular fluid into the fimbriated end of the Fallopian tube. The awaiting, or soon-to-arrive, spermatozoa approach the ovum at their usual rate of speed (about 0.05 mm. per second). Once the spermatozoa come in contact with the follicular fluid, they become accelerated in their motion. This process provides a more rapid meeting of the gametes than might otherwise occur. The meeting of a spermatozoon with the ovum is still a matter of chance. However, the spermatozoa are more rapidly brought into the immediate sphere of the awaiting ovum. The in vitro work reported in this paper, with use of follicular fluid, indicates that sperm drive can be accelerated 2 to 2½ times.

An induced increase in longevity of sperm, as has been reported with follicular fluid,[2] does not necessarily assure that the power of fertilization will be retained over the period of prolonged life span. The increased rate of sperm travel which is induced by the addition of follicle-cyst, hydrosalpinx, and peritoneal fluids should account for the arrival of the spermatozoa at the upper end of the Fallopian tube in a shorter period of time. In addition, a greater number of spermatozoa may travel the necessary course during the limited period when they are capable of fertilizing the awaiting ovum.

In clinical experience, subfertile men whose wives have conceived at least once have spermatozoa with one characteristic in common with the spermatozoa of men classified as highly fertile. In both groups, the speed of the spermatozoa is normal, although the number of moving cells is reduced in the case of subfertile men. Thus it appears that the speed (drive) of the spermatozoon is the feature most closely associated with its ability to fertilize. This closely corresponds with the feeling of Casares Ponce and Botella Llusia,[6] who reported the velocity (drive) of spermatozoa as the most important index of the fertilizing capacity of semen.

From the results of these in vitro studies, it appears that follicular fluid, hydrosalpinx fluid, and peritoneal fluid may serve as an aid to the barren couple. By the addition of one of these fluids to the semen sample, plus the use of intrauterine insemination, the number of active sperm required for fertilization may possibly be reduced to the barest minimum. Perhaps the man with only a few thousand active cells may, with these two aids, be capable of fertilizing his mate.

Summary and Conclusions

1. In vitro studies indicate that human follicular fluid (follicle-cyst fluid), tubal (hydrosalpinx) and peritoneal fluids have the ability to accelerate the drive (speed) of human spermatozoa.

2. The fluids are capable of producing this acceleration without deleterious effect upon the longevity or number of viable sperm. Longevity may be enhanced slightly.

3. No specific modus operandi has been found as yet to explain these actions.

4. The results of the studies suggest that, in man, follicular fluid plays a greater role in the physiologic reproductive mechanism than hitherto has been recognized.

5. The value of these fluids, together with artificial insemination, as an aid to the childless couple has been discussed.

Many thanks are due to Dr. E. J. Farris and Dr. R. A. Kimbrough for their guidance and supervision during the entire course of this project.

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PSEUDOTUBERCULAR GRANULATIONS OF THE UTERINE TUBE

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IT IS fairly common to find, in the subserosa of both Fallopian tubes, a series of small cystic formations, varying in number, the true nature of which, from their appearance at operation, may cause the surgeon justifiable concern. This concern arises from the risk of mistaking these lesions for tubal tuberculosis. The name "pseudotubercular granulation" (which is based entirely on the gross appearance of the growth, since from the histological aspect these two formations are totally dissimilar and cannot be confused with each other) implies this error in diagnosis which could occur during operation.

Macroscopic Appearance.—The lesion consists of small cystic formations, whitish in color, of varying diameter, though usually they do not measure more than 2 mm. across. The smallest of them may be compared to a grain of sand (Fig. 1).

The number of cysts also varies. Sometimes they are numerous, being spread irregularly throughout the tubal subserosa and having the appearance of a true granular tubercular growth. In other cases they are few in number.

Most frequently they appear on the surface of both tubes, directly beneath the peritoneum. They do, however, occasionally occur in the subserosa of the upper segment of the uterus, in other zones of the pelvic peritoneum, and—most rarely—in the omentum and the sigmoid flexure.

In addition to simulating tuberculous lesions, they may also have the appearance of a hydatidiform growth, or granulomas of foreign bodies such as talcum, lycopodium, sulfathiazole, etc.

Histology.—These formations correspond to small subserous cysts (Figs. 3 and 4). They satisfy perfectly the definition of cysts in pathological anatomy: a neoplastic-formed cavity lined with epithelium with a fairly dense liquid or semiliquid contents. The wall is made up of true stratified squamous epithelium, resting on a very thin base which separates it from the underlying tubal wall. It has no papillary formations and a very limited capacity for proliferation or hyperplasia, being in reality of a more secretory than productive nature.

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The epithelium is made up of various layers, particularly in the zones distant from the peritoneum. Only two, or at most three, layers are found in the wall of the cyst which is in contact with the peritoneum. In some cases the cyst wall and the serosa may become fused, forming a single lining which covers and surrounds the protruding part of the cyst.

The cyst always contains serum which may coagulate on the application of a fixing agent, but it has a low protein content. In colored preparations it appears as a deposit of hyaline material, taking on in parts a reticular shape.

Fig. 1.

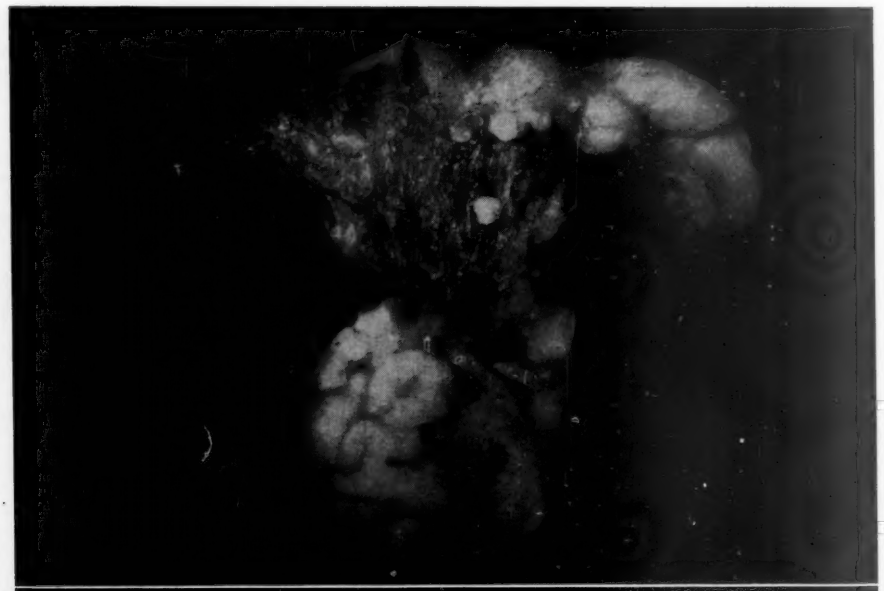

Fig. 2.

Fig. 1.—Specimen with pseudotubercular granulations in the Fallopian tube and in the mesosalpinx.

Fig. 2.—Fallopian tube with authentic tubercular granulations.

Behavior of the Uterine Tube.—How does the tube behave in this multicystic process? The lesion described has been found associated with varying conditions in genital pathology, such as pelvic congestion, uterine fibroids, etc. It can be ascertained, however, that it is not related to any type of genitopathological lesion. It often appears in tubes which are otherwise completely normal from the histopathological standpoint.

The tube behaves passively, sometimes showing, in the zones close to the cyst, particularly when the cysts are large, a certain degree of atrophy caused by compression.

In the histological preparations we have seen, there has not been any element of inflammation.

Fig 3.

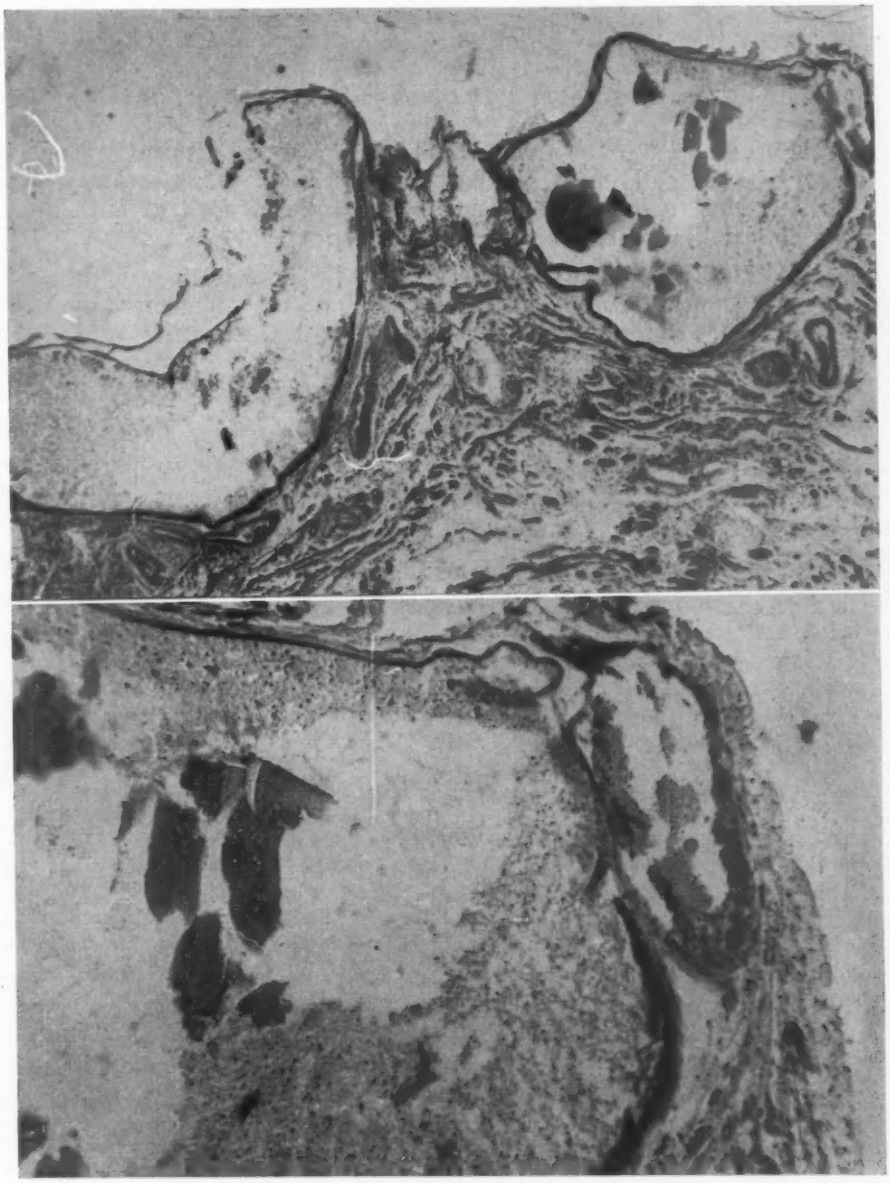

Fig. 4.

Fig. 3.—Histological section of two subserous cysts.
Fig. 4.—Small cystic cavity with a cellular deposit in one of the angles.

Histogenesis.—From the histogenetic point of view, this lesion has been attributed to inflammatory, traumatic, and congenital origins.

We are not inclined to the theory of inflammatory etiology because of the absence, at least in all the preparations studied by us, of any evidence of an

inflammatory process. With regard to the theory of traumatic origin, in the opinion of some, these formations correspond to small serous pinchings of unknown origin. We believe that they may be embryonic inclusions consisting of cells which have acquired secretory qualities, giving rise to the formation of cysts. Their origin might be compared with that of the so-called dental cysts arising from inclusions of ectodermal origin which occur in both the upper and lower jaws.

This suggestion would be better substantiated if we could find, in the histological study, epithelial islets of the same nature as the cells of the cyst wall but without the form of a cyst or at least with only the early stages of one. In one of the preparations studied by us, we noted the presence of a small cystic diverticulum (or a small independent cyst in its early stages) with a wall very rich in cells and poor in secretion (Fig. 4). Particularly in one of the corners of this little cyst there is a cellular deposit of multiple layers which has almost the appearance of a true cellular islet.

Practical Method of Diagnosis.—Finally, if there is any doubt as to the nature of this cystic process during operation, the surgeon may facilitate making the correct diagnosis by choosing the largest granulation and sectioning it through the middle, revealing its serous contents.

Summary

Pseudotuberculous granulations of the Fallopian tube, to which very little reference is made in textbooks, frequently present to the surgeon a problem in differential diagnosis.

Description is given of the gross and microscopic character of this process, with a discussion of various theories of histogenesis.

TORSION OF FALLOPIAN TUBE FOLLOWING TUBAL LIGATION

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TORSION of the tube is a rare condition seldom diagnosed preoperatively. Case reports have appeared in the literature since Bland and Sutton first described a case in 1890. The condition is particularly unusual in a tube free from disease. Torsion of the adnexa in practically all instances follows adnexal cysts or tumors. In 11 cases of torsion reported by Peerman and Williams[1] in 1954, there was only one twisted tube and ovary with no associated pathology. Robins[2] in 1954 reported 2 cases of torsion of a normal tube and ovary but these cases complicated pregnancy. In 1956 Jukofsky, Schretzmann, and Inceciyan[3] reported a case of torsion of the tube in a 15-year-old girl with complete absence of a mesosalpinx on the affected side. Kohl,[4] also in 1956, reported a case of torsion of a tube after a Pomeroy sterilization. The following is another report of torsion of a tube associated with a Pomeroy tubal ligation.

Case Report

Mrs. T. J., aged 29 years, para iii, was admitted to the Gynecological Service of the 1605th USAF Hospital on Nov. 18, 1957, with the chief complaint of pain in the right lower quadrant of 2 days' duration. Her last normal menstrual period was on Oct. 28, 1957.

The patient had awakened 2 days prior to admission with the sudden onset of a cramp-like pain in the right lower quadrant. Nausea and anorexia were present but there was no vomiting. That evening she was seen in the emergency room and a diagnosis of *Mittelschmerz* was made. The patient was given a sleeping tablet and was told to return if the pain persisted. The pain increased in severity and spread to involve the entire abdomen. Frequency of urination was present, but no dysuria. She had had a normal bowel movement on the previous day but none since. On the second day after the onset of pain, the patient returned to the hospital and was admitted. There was still associated nausea but no vomiting.

The past history revealed that 6 years prior to admission an elective tubal ligation had been performed in Arizona following her third normal pregnancy. An appendectomy had been performed in 1944 and a diagnostic curettage and cervical conization were done because of a "positive" Papanicolaou smear in September, 1956.

Physical examination disclosed a well-developed, well-nourished white woman in acute distress from severe abdominal pain. The vital signs were as follows: Blood pressure 114/62, pulse 94, temperature 98.2° F., respirations 22. On examination, the chest, lungs, and heart were within normal limits. Abdominal examination revealed generalized tenderness over the entire abdomen, but of greater intensity in the right lower quadrant. Rebound tenderness was elicited. There were marked muscle guarding and rigidity in the right lower quadrant. No masses were palpable. Pelvic examination showed no bleeding or discharges. A normal

cervix was noted and a uterus of normal size that was displaced to the left. A markedly tender, tense, movable, 6 cm. cystic adnexal mass was palpated on the right side. The mass extended into the right cul-de-sac. The left adnexa were negative.

Laboratory findings were as follows: White blood count 12,400 with 94 per cent neutrophils and 6 per cent lymphocytes, hemoglobin 15.3 Gm., and hematocrit 44 per cent. Urinalysis was negative. A chest x-ray and flat plate of the abdomen were within normal limits.

The preoperative diagnosis was torsion of a right ovarian cyst. At laparotomy an 8 cm. tense, blue-black, infarcted, edematous mass was noted to be present in the area of the distal segment of the right Fallopian tube. The fimbria were noted to be attached to the mass and confirmed the above impression. The right ovary was noted to be normal. A 2 cm. gap was present between the proximal and distal segments of the tube. The left adnexa were normal except for the absent segment of the Fallopian tube. The twisted mesosalpinx was easily clamped, cut, and ligated, and the stump was buried in the broad ligament.

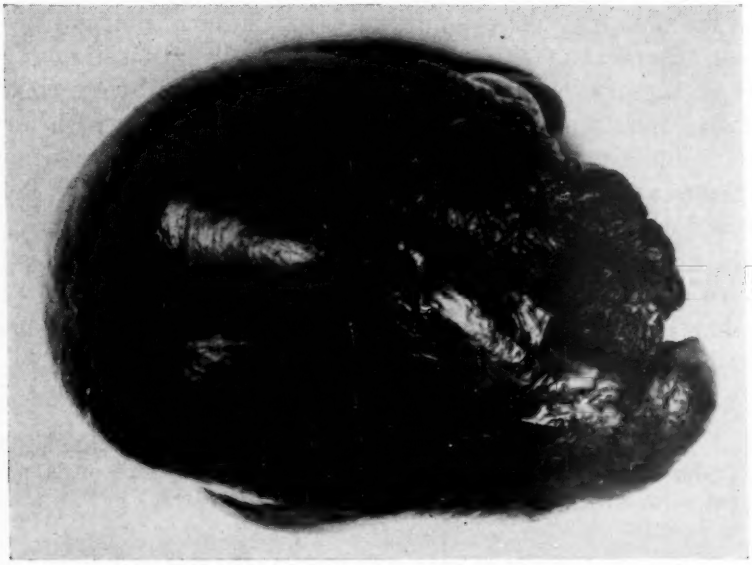

Fig. 1.—Gangrenous portion of the Fallopian tube removed at operation.

Pathological Report.—The specimen consisted of a soft, cystic, dark blue mass approximately 5 to 6 cm. in greatest diameter. The surfaces were smooth throughout. On cut section it consisted of slightly cloudy brown fluid. The specimen consisted of multilocular cysts with the largest cyst measuring approximately 2.5 to 3 cm. Several of these cysts, however, were joined. Compressed, somewhat thick, brown tissue was seen occupying one wall, measuring about 1 cm. in thickness. A section of the wall revealed a fibrous tissue lining infiltrated with a considerable amount of hemorrhage. There was a flat cuboidal-cell lining on the inside of this wall. The usual convolutions of the Fallopian tubes were compressed and only in rare areas were any unfoldings observed. In some areas the wall was infiltrated with polymorphonuclear leukocytes.

Comment

The predisposing factor in torsion of the adnexa is most likely any condition that results in a mass attached by a narrow pedicle for its blood supply. Whenever this state is encountered, whether it be from an ovarian cyst, hydrosalpinx, or a parovarian cyst, the diagnosis of torsion of the adnexa should

be suspected, when associated with an acute abdominal crisis referable to the lower quadrants. The Pomeroy technique for tubal sterilization is deservedly considered a good procedure, but it should be recalled that the conditions just described can result from the Pomeroy technique. The gap in the tube allows the distal mesosalpinx to act as a pedicle and the possibility of torsion increases. This is especially true, as stated by Kohl,[4] when associated with a long mesosalpinx. The fimbriated segment of the tube lies free and may swing and twist, thus producing torsion. This is the second case report of torsion of a tube following a Pomeroy sterilization.

Since the Pomeroy procedure is so common, this complication is indeed an unusual one. The gynecologist should suspect the diagnosis of torsion of a tube, however, when the symptoms noted in the case report are present.

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PELVIC PHLEBOGRAPHY*

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THE technique of pelvic phlebography, first described by A. de la Peña,[7] improved by Ducuing and associates,[8] and further refined by Guilhem and Baux,[10] has become the subject of increasingly intensive study.[1, 13, 18, 19]

Visualization of pelvic veins can be done by any of three routes: through the pelvic bones, directly into the veins, or by intrauterine injection. Guilhem and Baux, for example, using the approach of the pelvic bony structures, showed the importance of the osseous drainage, its centripetal direction, and the independence of the visceral circulatory currents in spite of the numerous anatomic anastomoses. By their work with all three methods, they described three main visceral currents: vesical, rectal, and genital. By the intrauterine route, it is possible to study only the genital current.

The present report deals principally with visceral circulation as it applies to the problems of pelvic congestion[2, 3, 5, 6, 11, 14-17, 20] and pelvic varicocele.[20]

Methods

Seventy cases were studied, 10 by the pubic approach and 60 by the intrauterine approach.

Pubic Approach.—This was employed not only in normal cases, but also in cases of cervical and endometrial malignancy. Its principal interest lies in the study of pelvic thrombophlebitis and in neoplasms which have extended to the pelvic walls.

The best site for the osseous puncture is the external surface of the pubis, 1 cm. below the upper border and 1 cm. from the symphysis. After the area is shaved and disinfected, it is infiltrated with 1 per cent procaine, and a No. 17 B-D needle is introduced into the bone by light taps with a small surgical hammer. Blood appears at the bottom of the needle, and 20 c.c. of a triiodine contrast medium is injected within a 10 second interval, the x-ray film being taken when the injection is completed.

Intrauterine Method.—This approach was utilized in cases of pelvic congestion, as well as in cases of myomas, ovarian cysts, and chronic pelvic infections. It does not require hospitalization. The patient is instructed to fast on the morning of the examination. She receives an antispasmodic suppository 30 minutes before the procedure. She is placed in the lithotomy position, the vagina is prepared with Merthiolate, and a cannula is introduced until it comes

*The present report is part of a larger study of pelvic circulation which is being carried out in the clinic of Prof. Dr. J. J. Crottogini.

in contact with the uterine fundus. A needle which is 2 to 3 mm. longer than the cannula is inserted through the cannula, thus penetrating the myometrium by this distance (Fig. 1).

Before the injection of the contrast medium, 150 units of hyaluronidase in 1 c.c. of saline solution is injected through the needle. (The addition of hyaluronidase to the procedure appears to have improved the results obtained. One of the difficulties of the method as originally described is the resistance of the myometrium to the 20 c.c. injection of the fluid. This resistance is largely obviated by the preliminary use of hyaluronidase.)

There is practically no pain if the contrast medium has a pH of 7 (as do Urografin 76 per cent or Hypaque 50 per cent, the most satisfactory agents employed in this study[18]). The first x-ray plate is taken during the injection of the last cubic centimeter of opaque medium; and, if seriography is being done, the succeeding plates are taken at intervals of 20 seconds. The passage of the contrast medium into the pelvis is very rapid; sometimes the needle punctures a large myometrial vein (Fig. 5), but it is also possible that the pressure of the injected liquid ruptures some of the numerous small vessels. The x-ray technique is the same as that of hysterosalpingography.

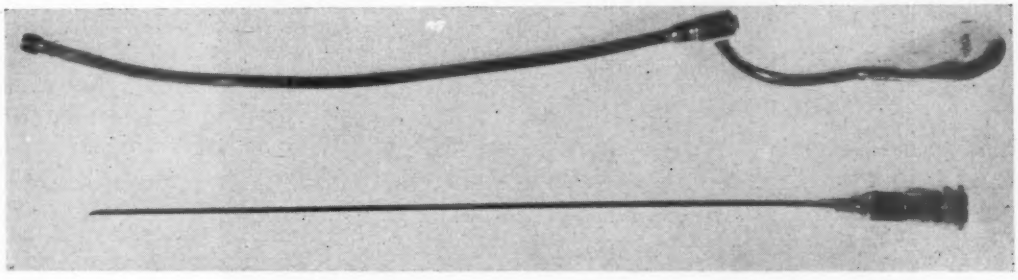

Fig. 1.—Cannula and needle.

Results

Normal Uteri.—Fig. 2 shows a phlebogram made by puncture of the left pubis, in which one may see the parietal circulation of the left pelvic wall. The contrast medium reaches the femoral vein by means of a retrograde anastomosis, but the principal drainage route is represented by a conspicuous obturator plexus, which forms a thick hypogastric vein. From this rises an important presacral plexus which supplies in part the right hypogastric vein. Some 4 or 5 cm. of the left common iliac vein is visible. This is a normal left pubic phlebogram; in cases of venous drainage difficulties, a rich anastomotic plexus with the circulation of the opposite side may appear.

Fig. 3 (Case 14) shows a normal intrauterine phlebogram. There may be seen the outline of the uterus, which in this case is deviated to the right. The vascular network of the uterus is apparent. The ovarian and uterine pedicles are normal; the vessels are thin and have no tortuosities, both important signs to note.

Fibromyomas of the Uterus.—Fig. 4 (Case 22) shows a phlebogram in a case of uterine fibromyomas. Practically all of the contrast medium drained to the left side, where there is seen a great helicoidal varicocele of the left uterine pedicle secondary to the fibroid. Apparently the needle punctured a large vein in the myometrium, for the smaller vessels are not visible. The results are variable in fibromyomas, and phlebography is only an auxiliary method in diagnosis, revealing the state of the venous circulation. In Fig. 5, there are small fibroids which have practically no influence upon the veins.

Fig. 2. Fig. 3. Fig. 4.

Fig. 2.—Case P7. Normal pubic phlebogram.
Fig. 3.—Case 14. Normal intrauterine phlebogram.
Fig. 4.—Case 22. Uterine fibroid. Helicoidal varicocele of the left uterine pedicle. Presacral plexus.

Chronic Infections.—This method gives a clear impression of congestive states of the internal genital organs. In cases of chronic infections, great varicosities often develop in the ovarian or uterine pedicles, and the uterus itself becomes congested. These are cases of secondary congestion, as also occurs with fibromyomas and certain retrodisplacements of the uterus.

Fig. 6 (Case 36) shows a varicocele of the left ovarian pedicle; note the rather wide separation of the numerous veins which constitute this abnormal pedicle. The right ovarian pedicle is not visible because the patient had had a right salpingo-oophorectomy a few years previously. This figure also shows a well-visualized uterine network, and on the right there is seen a double hypogastric vein, which receives the blood of the varicose uterine pedicle.

Pelvic Congestion.—The most clear-cut results have been in cases of true primary congestion.[3, 4, 6, 9, 14, 20] This congestion may be limited to the uterus, or to one or both pedicles; and the varices represent a late stage in the development of the condition.[2, 6, 14, 20]

Fig. 7 (Case 42) shows congestion confined to the uterine body, both ovarian pedicles being normal, and the uterine pedicles also normal except that the right one has a tendency to varices. There is a presacral anastomosis between both hypogastric veins, and the hypogastric veins may be followed as far as the common iliac veins and the inferior vena cava. The diagnosis of uterine congestion was confirmed at laparotomy, and also reinforced by an unusually slow disappearance time of radioactive isotope injected into the myometrium.[6, 12]

Fig. 8 (Case 44) shows a congested uterus and varicocele of the right ovarian pedicle. The left pedicles are not visible. Clinically the patient complained of pain in the right lower quadrant without signs of organic disease. In Fig. 9 (Case 46) the patient had lower abdominal pain and hypermenorrhea, and the phlebogram showed a very large varicocele of the left pedicles, which are enormous in comparison with those on the right.

Serial X-ray Technique

The foregoing findings present a static aspect of pelvic circulation. But pelvic circulation is a dynamic process, and therefore seriography should give significant further information. The introduction of a seriographic technique offers a new view of circulatory function in the pelvis. The best results are obtained by taking the x-rays every 20 seconds.[19] The normal time in which the contrast medium disappears is about 20 seconds, which means that usually in a second plate, taken 20 seconds later, the veins are not visible. Thus one may speak of a slow "time of disappearance" when in a second and a third plate the pelvic veins are still visible. By this method it was demonstrated that, in spite of the presence of varicose veins, the circulation can be normal in certain cases, but in others there was noted persistence of the contrast medium in the veins for a minute or more.

Figs. 10 and 11 (Case 51) show a normal disappearance time. The first plate visualizes drainage toward the right side, practically normal except for a slight uterine varicose vein. In the second plate, taken 20 seconds later, practically all the contrast medium has disappeared.

A delayed time of disappearance is demonstrated in Figs. 12, 13, and 14. The first plate shows a congested uterus with varicocele of the broad ligaments, especially the right one. The ovarian pedicles are normal. In Fig. 13, taken 20 seconds later, the uterine vessels are full of contrast medium and show dilatations; the varicocele is still apparent, emptying slowly. In Fig. 14, the uterine vessels are still visible, which indicates the degree of intensity of the vascular congestion; the right varicocele persists unchanged.

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 5.—Case 9. Congenital absence of left ovarian pedicle. Small fibroid (arrow). No varicose veins.
Fig. 6.—Case 36. Varicocele of the left ovarian pedicle. Right ovarian pedicle not visible. Double hypogastric vein at right.
Fig. 7.—Case 42. Congested uterus, with normal pedicles. Great pelvic vessels visible.

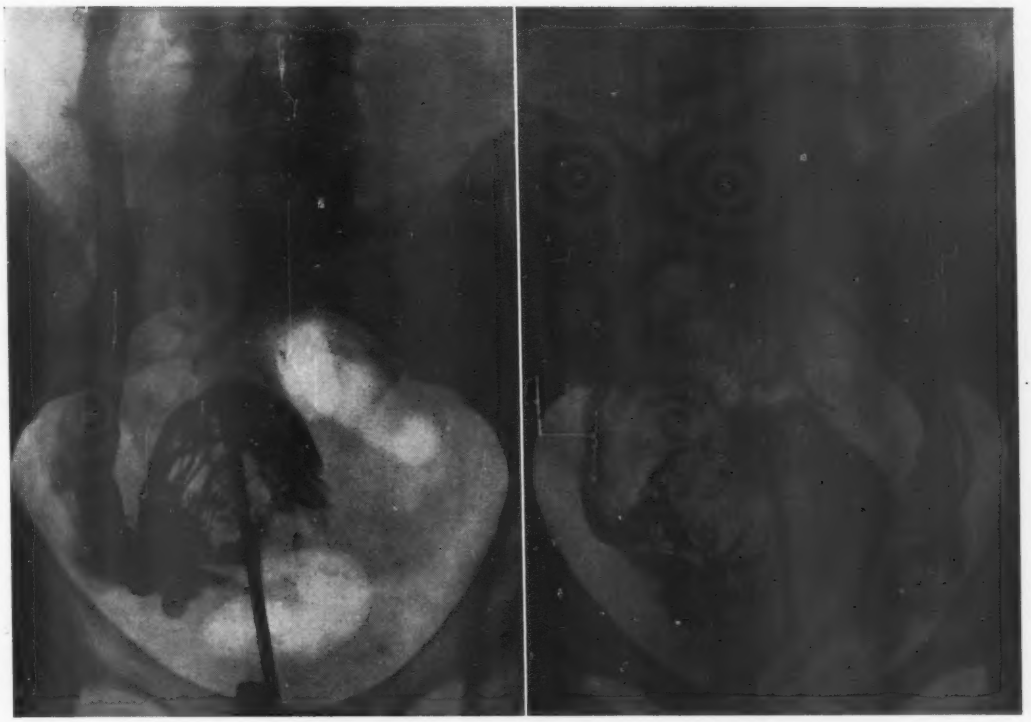

Fig. 8. Fig. 9

Fig. 8.—Case 44. Congested uterus. Varicocele of the right ovarian pedicle.
Fig. 9.—Case 46. Varicocele of both left pedicles.

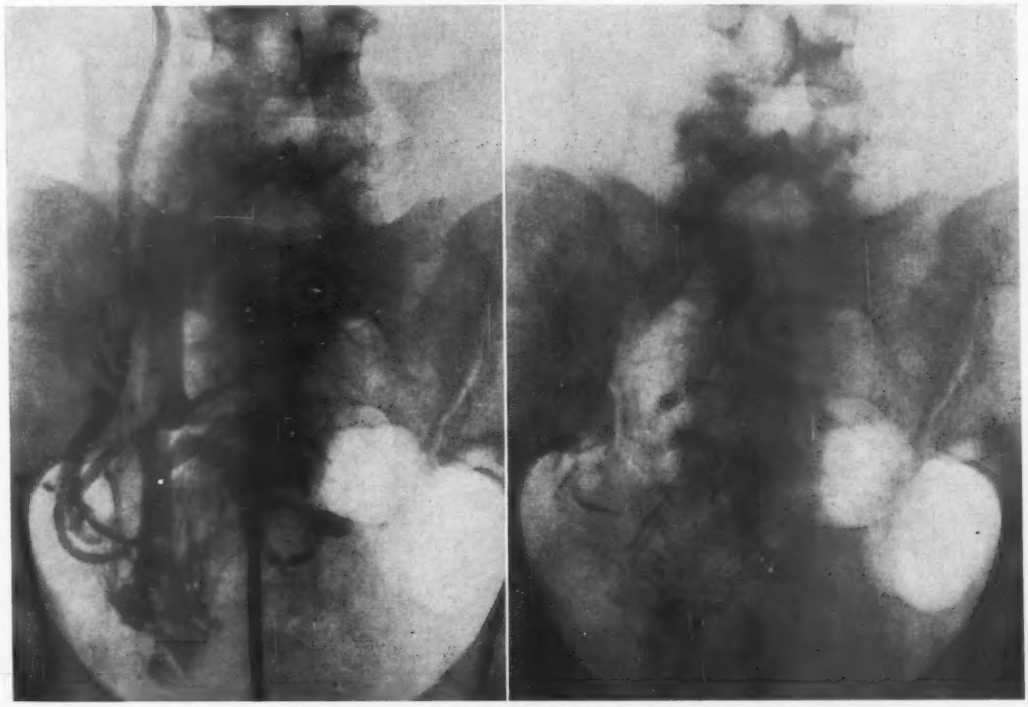

Fig. 10. Fig. 11.

Fig. 10.—Case 51. Normal case. Drainage to the right.
Fig. 11.—Case 51. Normal case. Twenty seconds later, practically all of the contrast medium has disappeared.

Fig. 12. Fig. 13. Fig. 14.

Fig. 12.—Case 58. Severely congested uterus. Left ovarian pedicle normal. Right ovarian pedicle not visible. Slightly varicose uterine pedicle at left. Large varicocele of the right uterine pedicle.

Fig. 13.—Case 58. Twenty seconds later. The uterine vessels are full of contrast medium. Varicocele still visible.

Fig. 14.—Case 58. Twenty seconds later. Varicocele without change. Uterine vessels still visible.

Seriography also is of some use in confirming the validity of the picture which appears on the first plate. For example, sometimes some of the vascular branches do not appear in the phlebogram. Many seriographic studies in this series have shown that ordinarily a vein which does not appear in the initial plate will not appear in a second or third one. Some such failures of visualization are due to congenital or acquired anomalies. Fig. 5 (Case 9) is an example of congenital abnormality in which the right ovarian pedicle cannot be seen.

Comment

The original purpose of this study was to evaluate pelvic congestion by the methods under discussion. These methods have been particularly useful in diagnosing pelvic varicocele, which has been demonstrated frequently in instances of pelvic congestion of long duration, a state more often discovered at laparotomy than suspected preoperatively. Many women with low abdominal and back pain, without signs of organic disease, have pelvic congestion,[3, 4, 6, 7, 14-17, 20] and many have pelvic varicocele.

It became apparent, as the study progressed, that seriography is a valuable method for the dynamic evaluation of the visceral pelvic circulation. Seriography could be further refined through radiocinematographic techniques, thus giving a more complete picture of the circulation.

The method gives helpful auxiliary information in cases of fibromyomas of the uterus and chronic pelvic inflammation.

Summary

1. The methods of pelvic phlebography are presented, with special emphasis upon the intrauterine route.

2. A modification of the original technique is presented, which consists of the injection of a hyaluronidase solution prior to the injection of the contrast medium.

3. Normal pubic and intrauterine phlebograms are shown.

4. The results are presented in the presence of fibroids, chronic pelvic inflammation, and especially in pelvic congestion, revealing a new method in the diagnosis of varicocele.

I wish to express gratitude to Dr. Charles H. Hendricks, Western Reserve University, Cleveland, Ohio, from the Sección Fisiología Obstétrica, Montevideo, Uruguay, for his valuable contribution in the translation and presentation of this work.

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Avenida Brasil 3105, Ap. 12

CORTISONE-INDUCED PROLAPSE AND INVERSION OF THE UTERUS IN MICE*

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IN THE course of a series of experiments centered about cortisone-induced congenital anomalies, some pathologic changes in the reproductive tract of the parturient mothers were observed.

This series of experiments had earlier shown that relatively massive doses of cortisone administered to pregnant mice frequently caused them to resorb the fetuses.[1, 5] When the pregnant females were treated with sub-resorptive doses of cortisone, the young developed various congenital anomalies. Cleft palate was produced with ease and regularity. Stillbirths were abundant and birth weights were seriously reduced. Congenital cleft palate has also been induced in the offspring of rabbits which received cortisone during pregnancy.[3]

All of the aforementioned findings emphasize the cryptic crippling powers of cortisone administered during a pregnancy. This report concerns deleterious effects on the pelvic organs of parturient mice.

Materials and Methods

The mice used in these experiments were raised in the mouse colony of the Department of Genetics, McGill University, on a diet of Purina fox chow and water ad libitum supplemented twice a week with bread, milk, and lettuce.

Five genetically different stocks of *Mus musculus* were used: (1) A; (2) a stock carrying the mutant "Naked" (N); (3) C57 BL-at; (4) C57 BL/6 Jax; (5) a genetically heterogeneous stock.

Pregnant females were isolated in individual cages until at least 2 days after parturition.

The cortisone used in these experiments was the Merck Cortone preparation. All injections were given intramuscularly in the quadriceps muscle.

Experimental Report

One hundred and sixty-five female mice were treated with cortisone during pregnancy. Of the 27 cortisone-treated females of stock N, 9 developed inversion or complete prolapse of the uterus and vagina within 2 days after parturition. None of the 138 cortisone-treated females of the other four stocks developed such conditions.

*This investigation was supported by NRC (Canada) grant H. R. 28, Ap. 1.

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Table I shows that the condition was induced by large doses, and by a dose so small (0.625 mg.) that none of the newborn mice had cleft palate. Treatment begun as early as the tenth day of pregnancy and as late as the eighteenth day caused prolapsed or inverted uterus and vagina in some cases.

TABLE I. NINE MICE IN WHICH INVERSION OR PROLAPSE OF THE UTERUS AND VAGINA DEVELOPED FOLLOWING PARTURITION

MOUSE	DAILY DOSE CORTISONE IN MG.	NO. DAYS TREATED	DAY OF GESTATION AT FIRST TREATMENT	NO. OFFSPRING IN LITTER	NO. OFFSPRING WITH CLEFT PALATE
a	0.625	4	10	2	0
b	0.625	4	13	6	0
c	1.25	4	11	8	7
d	1.25	4	13	6	1
e	2.5	4	13	4	2
f	2.5	4	14	6	0
g	2.5	5	11	6	2
h	10.0	1	10	3	3
i	10.0	1	18	8	0

Comment

The spontaneous incidence of prolapse and inversion within the N stock is estimated to be not more than 1 per cent,[4] which is very much lower than the 33 per cent resulting from cortisone treatment. The mechanism of spontaneous development of these conditions in mice is not well understood, and no report about it has been seen by the writer.

Ingle[7] asserted that a catabolic action of adrenal cortex steroids must be involved to explain the very rapid breakdown of some tissues. Many reports have since supported the likelihood of cortisone-induced catabolism. It may be that connective tissue in the ligaments supporting the uterus is seriously affected by the strongly catabolic action which cortisone exerts on some tissues.

It has been reported in this series of experiments that resorption of embryos, diminished mean birth weights, reduced size of litters, and frequent stillbirths all occurred with remarkable frequency. These findings also might be considered to be the result of severe catabolic manifestations of cortisone treatment during pregnancy. In these cases, however, such catabolic results might in turn be due to repression of anterior pituitary activity[8] or an antagonizing effect upon sex hormones by the cortisone, thus preventing successful pregnancies.

The response to cortisone treatment is strongly influenced by the underlying genetic makeup of the animal receiving treatment. This was revealed in the past by studies on the incidence of cortisone-induced cleft palate. There, well-defined differences between mice of different stocks were observed in response to identical cortisone treatment.[2, 5, 6] Presently, one thing seems to be certain. There is a genetic difference between stock N and the other four stocks used in these experiments with regard to the development of puerperal inversion and prolapse of the uterus after cortisone treatment during pregnancy. Where this difference expresses itself is not known. We

might suggest that in females of stock N the ligaments supporting the uterus are more sensitive to cortisone than those of the other four stocks. On the other hand, perhaps a difference in sensitivity to cortisone is not involved here. In the N stock these ligaments may frequently be degenerate or poorly developed as a result of inheritance, but not quite weak enough to permit a prolapse. Cortisone may be an agent which causes the ligaments to "pass their threshold of critical weakness," and result in prolapse or inversion of the uterus in some cases.

To the mounting list of undesirable effects of cortisone we may now add postpartum inversion and prolapse of the uterus and vagina in mice.

Summary

Postpartum inversion or complete prolapse of the uterus and vagina were frequently seen in one stock of mice given cortisone treatment during pregnancy.

I am grateful to Professor F. C. Fraser of McGill University for his guidance and friendship during the project, to Professor F. L. Hisaw of Harvard University for appraising the manuscript, and to Dr. J. H. Laurie of Merck & Co., Inc., for supplying the cortisone.

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THE USE OF URINARY SEDIMENT AS AN AID IN ENDOCRINOLOGICAL DISORDERS IN THE FEMALE

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VAGINAL smears have been useful for many years in the study of endocrine disturbances and of cyclic changes in the genital tract. The cytological changes in the menstrual cycle, in estrogen therapy, and in the menopause are familiar to all.

In the course of study of urinary sediment, cells were found in catheterized specimens which mirrored the changes in cells obtained concurrently from vaginal smears. While the number of cells for study was sparse, the cells, nevertheless, could be accurately diagnosed. When urine was obtained by the use of a "bird-feeder," more cells were obtained. Voided, noncatheterized specimens, of course, contained cells washed from the vulva as well as exfoliated urethral and bladder epithelium.

The vaginal and bladder epithelium is derived from the urogenital sinus. The sinus epithelium creeps up into the vagina until eventually the vagina and portio vaginalis of the cervix are covered by epithelium of the sinus urogenitalis. The original mesodermal islet at the base of the urinary bladder is also replaced by the encroaching sinus epithelium which eventually lines the urethra and the trigone of the bladder.

The material used in this study is from the gynecological and obstetrical services of the French Hospital. No attempt at statistical appraisal was made. The purpose of the study was to determine whether or not the bladder epithelial cells confused the cytological picture. The use of urinary sediment for cytological study has also been reported by Lencioni.[1] Papanicolaou and Shorr[2] showed the effect of estrogen on the vaginal cytology. In 1940 Shorr[3] demonstrated that the cytological findings characteristic of pregnancy were due to estrogen plus progesterone. We studied the urine of 50 women in the menopausal age group and found the usual small, round, nucleated cells with a large number of leukocytes typical of this condition. When the patients were treated with estrogen, the vaginal smears and the urinary sediments showed an increase in the number of large "pavement" cells with a paucity of leukocytes. Our problem in the interpretation of urinary sediment is the same as with vaginal smears, that of distinguishing pyknotic from translucent or vesicular nuclei. Using the phase-contrast microscope after the method of Wied,[4] we

Fig. 1.

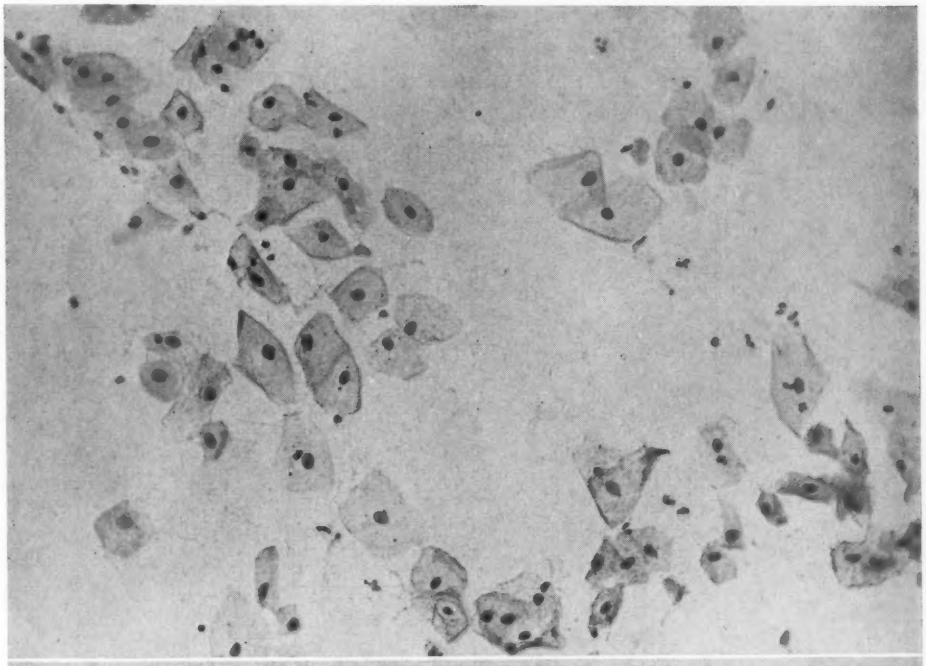

Fig. 2.

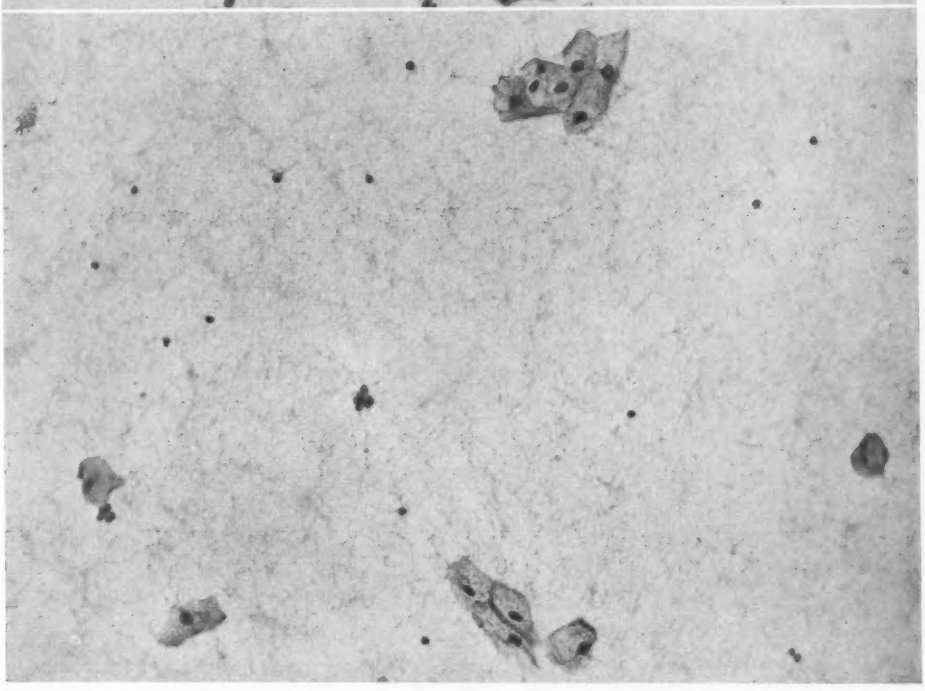

Fig. 1.—Vaginal smear in a pregnant woman, aged 28, experiencing bleeding. The smear shows response to estrogen with cells of the premenopausal group and numerous basement cells. The patient went on to term.

Fig. 2.—Cells obtained from the bladder sediment of the same patient as Fig. 1, showing a marked similarity to the vaginal smear.

found the urinary sediment cells and the cells of the vaginal smears to have the same karyopyknotic index. We have used the urinary sediment as an indication of hormone levels (Figs. 1 and 2). The urines of patients admitted to the obstetrical service and those admitted for inevitable abortions were contrasted. We have found the use of urine sediment valuable in studying the abnormal cells as reported by Pierce and Cope[5] and Pierce.[6] The abnormality

Fig. 3.

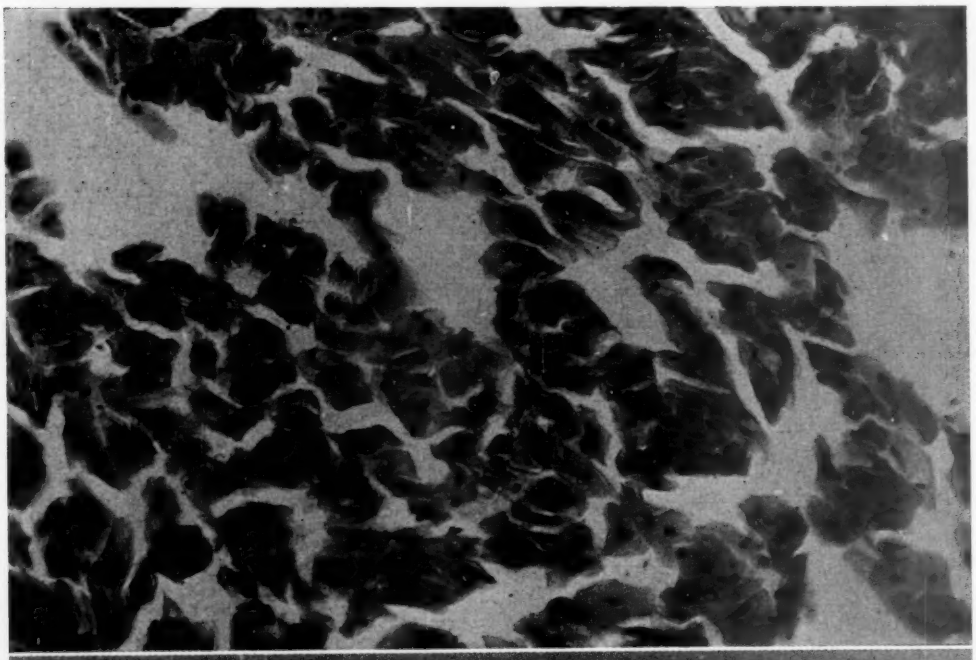

Fig. 4.

Fig. 3.—Vaginal smear from a pregnant woman who subsequently had an abortion. The smear shows predominantly the superficial type cells which are considered abnormal in pregnancy.

Fig. 4.—Cells from the bladder urine of the same patient as Fig. 3, showing similar superficial type cells.

consists in an increase in acidophilic, estrogenic, or superficial cells and a decrease in basophilic or intermediate type cells. Pierce considered the vaginal smears abnormal when they showed more then 30 per cent of superficial type cells (Figs. 3 and 4). In our group of obstetrical patients we have found similar percentages in the cells found in the urinary sediment.

Fig. 5.

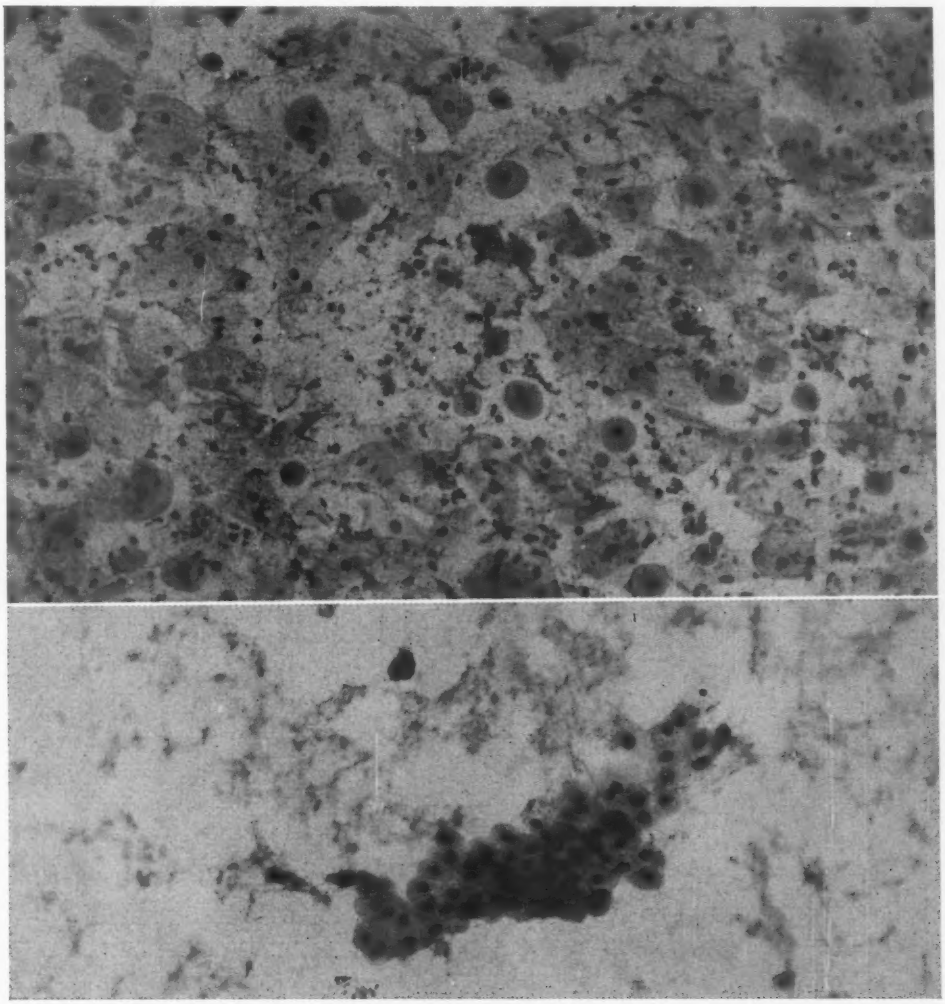

Fig. 6.

Fig. 5.—A vaginal smear in a case of senile urethritis with typical postmenopausal groupings of the cells.

Fig. 6.—Cells from the urinary sediment smear of the same patient as Fig. 5.

Urinary cytology studies were performed on 20 patients with senile urethritis. Estrogen therapy was given to all 20 patients. In 12 patients with good cytological response the clinical symptoms were alleviated. We have found this method of urinary cytology valuable for following the course and prognosis in cases of senile urethritis (Figs. 5 and 6).

Summary

The epithelium of the vagina, urethra, and trigone is derived from the urogenital sinus. Exfoliated cells from these areas are similar in appearance and change with hormone stimulation.

Examination of the urinary sediment is valuable in young girls in whom vaginal examination may be believed to be too traumatic psychologically. It is also of value in cases of hemorrhage which would obscure the vaginal cytology or when repeated examinations are necessary.

We have become particularly interested in the urinary sediment of pregnant women. If, as seems to be the case, a smear showing more than 30 per cent of abnormal cells indicates that miscarriage is probable, perhaps obstetricians should add this examination to the prenatal list.

Urinary cytology studies are important in cases of senile urethritis as a measure of prognosis and therapy.

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UTERINE POLYP FORCEPS AND CURETTAGE

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VARIOUS probes, sounds, forceps, and curettes have been employed by the "keyhole surgeons" to explore, curette, biopsy, and pack the uterus ever since Recamier[4] invented the curette in 1846. The use of the curette for the diagnosis and treatment of abnormal uterine bleeding is a well-established practice. Stander, Javert, and Kuder[7] studied 3,466 such cases in 1942 and found endometrial polyps in about 10 per cent. Subsequent follow-up disclosed that some of these patients continued to bleed after as many as 2 or 3 curettages, because of persistent polyps as shown by hysterectomy.

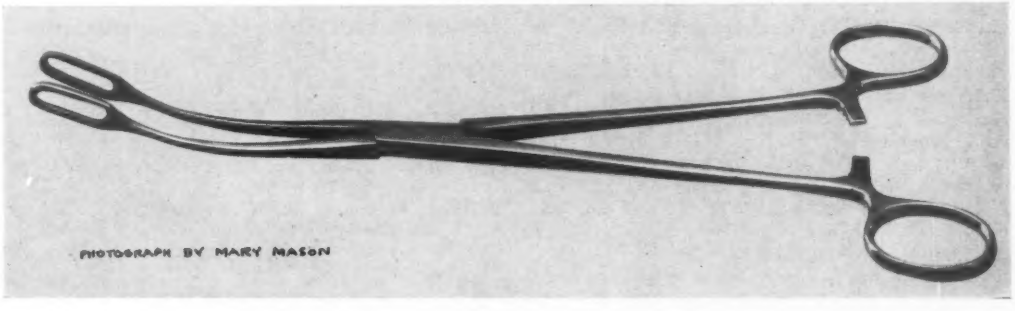

Fig. 1.

As obstetrical and gynecological pathologist, I have had the opportunity of examining many of these uteri, and in 1947 this experience led me to modify an ordinary 9½ inch curved sponge forceps by decreasing the transverse diameter of the fenestrated portion from ½ to ¼ inch. This modification permitted the forceps to enter the internal os more readily than the larger ovum or placenta forceps, especially when the uterus was small and atrophic. This instrument* is shown in Fig. 1. It is similar to the DeLee[1] ovum forceps which, however, is straight while this instrument has a "pelvic" curve.

Technique and Uses

After dilatation of the cervix and before the use of the curette, the uterine polyp forceps is gently introduced through the internal os. It is immediately opened and then is thrust gently upward if the uterus is anterior. It is then closed and is rotated slowly as it is withdrawn. Experience will indicate

*Manufactured by the Masters Surgical Instrument Company of New York City.

whether a polyp has been "caught." If so, rotation of the forceps is continued, as it is gently withdrawn from the uterine cavity. The forceps is then reinserted, turned, and removed several times in various directions until the operator is satisfied that no endometrial polyps are present, or that all of them have been removed.

Employing this technique, I recently removed 3 polyps from a patient who had been curetted a short time before by a capable gynecologist in the usual manner. A uterine septum was diagnosed in another case by this method.

This forceps is also useful following curettage to remove endometrium and blood clot that have collected above the internal os. It has replaced the placenta forceps for removing retained secundines since the cervix need not be dilated as much, thereby preventing a possible "incompetent os" in a subsequent pregnancy. Occasionally polyps have been found with this instrument in patients treated for sterility. It also facilitates the removal of cervical polyps in the office because of its length and gentle grasp of the polyp. According to Rust,[6] it should appeal to gynecologists who do curettages in their offices.

Finn[2] recently advised routine curettage prior to all vaginal and abdominal procedures but failed to advocate using a polyp forceps. Josey[3] has currently described several years' experience with forceps exploration at curettage with the use of the Randall kidney-stone forceps.[7] I prefer my instrument and it is much cheaper. It has been favorably received by the surgeons at New York Hospital and Woman's Hospital as well.

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KNEE REST APPARATUS FOR THE CULDOSCOPY PATIENT

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IN PREVIOUS reports,[1-5] mention was made of the use of a knee rest apparatus with a modified Buie position to place a patient better for culdoscopic examination. The idea of such an apparatus was first brought to our attention by Dr. Albert Decker.[1] As described in his monograph, a modified Buie position with a flat platform was very satisfactorily employed. In cases where cul-de-sac anesthesia is by local injection, with or without paracervical or pudendal block, this method of placing the patient is very satisfactory. When other forms of anesthesia are used (saddle, caudal, gas-oxygen-ether), it is necessary to employ an apparatus such as that described by Brown and Bear[4] or the classic leg holders employed by Decker.

This department has been asked by various endoscopists to publish a description of the knee rest which was devised at this institution several years ago.

The knee rest consists of the ordinary operating table foot plate with the addition of the aluminum components shown in Fig. 1. The dimensions of the parts are given. The weight-bearing surfaces are covered with a sheet of 2 inch foam rubber held in place with tape. A cotton blanket could be used for this purpose. The entire apparatus is then covered with rubber sheeting which is stitched in place. This permits cleaning of the knee rest as necessary without disturbing the foam rubber padding. It insures maximum comfort of the patient. It also prevents injury from undue pressure over the knees and lateral peroneal surfaces. The aluminum side pieces permit proper positioning of the patient's knees with optimal abduction and internal rotation of the thighs. Thus there is the added advantage over just the foot rest itself in that the patient under regional or general endotracheal anesthesia does not require mechanical braces or straps over the thighs or calves or human leg holders to maintain the thighs in flexion and proper abduction. With the shoulder braces and the table positioned as shown in Fig. 2, the patient can be comfortably and adequately maintained for 45 minutes to an hour if necessary. A rough rule of thumb is applied when determining the height of the platform from the break in the table. This distance is approximately one half the length of the patient's thigh. This distance would be modified depending on the obesity of the patient inasmuch as there must be adequate space between the patient's abdominal wall and the table, to permit an adequate pneumoperitoneum for visualization and displacement of viscera from

the pelvis. In addition, palpation of the abdominal wall is frequently required. This knee rest permits culdoscopy to be performed with only the operator and anesthetist present.

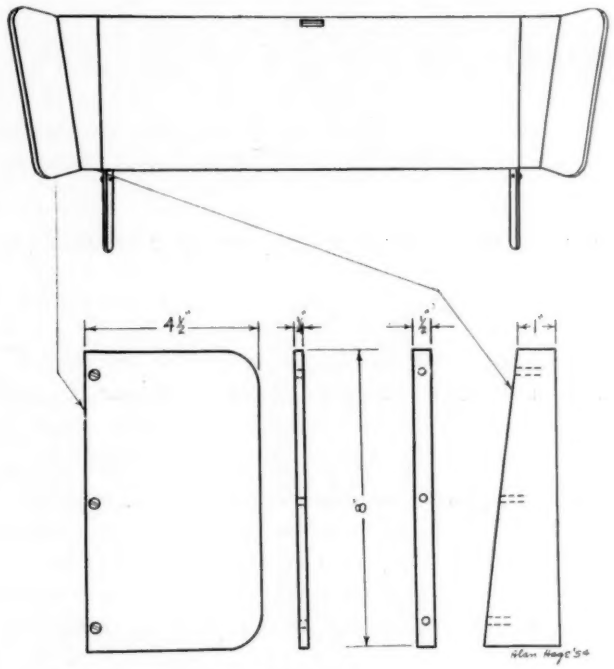

Fig. 1.

Fig. 2.

Summary

An apparatus for use in culdoscopy has been presented. This apparatus has been employed over 1,000 times and has proved to be very satisfactory.

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Obstetrics

SOME OBSERVATIONS ON THE HISTOLOGY OF THE HUMAN OVARY DURING PREGNANCY*

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THE writings of others regarding the human ovary during pregnancy have been previously presented.[15] The reader is referred to that study for a historical review preliminary to the following dissertation. A second article[5] was concerned with the decidual reaction seen in ovaries from pregnant and nonpregnant patients. The present study deals primarily with our observations on the corpus luteum and follicular structures in the ovary of the pregnant woman. A brief comparison of the corpus luteum during pregnancy and so-called "corpus luteum cysts" will also be made.

Material and Methods

A wedge-shaped biopsy was removed from the free or convex surface of one or sometimes both ovaries in 43 patients operated upon for various indications. Thirty-nine of these patients were pregnant, and 4 were within 2 weeks post partum. The biopsy material was immediately fixed in the operating room with Bouin's fluid. In addition, ovarian tissues were on file in the laboratory from 11 other pregnant patients and from 2 recently delivered patients. Thus, a total of 50 ovarian specimens from patients with intrauterine pregnancies and 6 from patients within 2 weeks of delivery were available for study. The duration of the pregnancies (by menstrual history) ranged from 5 weeks to term. Routine sections of ovaries were available also in the laboratory files from 24 patients with tubal pregnancies. Eighteen were proved by the concurrent demonstration of trophoblastic elements. Again taken from

*Supported in part by a cancer control grant from the National Cancer Institute of the National Institutes of Health, United States Public Health Service.

the general laboratory files, sections from 48 "corpus luteum cysts" were reviewed. Most of these routine materials had been first fixed in 10 per cent formalin and then placed in Bouin's solution for a day previous to blocking.

All sections were stained with hematoxylin and eosin. In addition, a representative group were prepared with the periodic acid leukofuchsin Schiff reaction technique suggested by McManus,[10] Wilder's modification of the reticulum stain given by Mallory,[11] and the Milligan trichrome stain.[14] Frozen sections were prepared from 12 of the specimens and stained with sudan IV for fat.

Although gross findings were noted when the material was personally secured, the results of the microscopic examination will be used as the basis of this report.

Since we have no specimens from the first 2 weeks of pregnancy, the reader is referred to our summary of the literature relative to such specimens (Table II[15]).

The ages of all specimens have been computed from the date of onset of the last normal menstrual period. On this basis, 15 specimens are from a 40 weeks' gestation, 8 are from 38 weeks', 4 from 37, 2 each from 6, 7, 8, 9, and 34 weeks', and one each from 5, 10, 12, 13, 15, 16, 27, 35, and 39 weeks' gestations. Therefore, 16 specimens are from the fifth to the thirteenth week of gestation. Three are from the second trimester. The remainder are from the thirty-fourth week to term. Because of the inadequate sampling of material from the second trimester (which is a direct outcome of lack of clinical indications requiring interruption of pregnancy at this time) these 3 specimens are included in our discussion with those of early pregnancy. The resulting two groups are divided, therefore, at the twenty-eighth week of gestation. It will later be seen that such a division is more than artificial; for many histological characteristics are present predominantly in one or the other of the two groups.

In almost every case, measurements of the newborn after the twenty-eighth week were available. In 10 of the 19 from early pregnancy (Group 1) the fetus was measured. The length of gestation computed by a method suggested by Arey[1] coincided reasonably well with that found by the use of the date of the last menses.

Results

Corpus Luteum of Pregnancy.—

General.—Corpora lutea of menstruation and pregnancy are very similar in structure. This is as would be expected, for the latter is in essence the outcome of continued growth and development of the former. Differentiation between the two is one problem with which the present study is concerned. Out of 50 ovarian specimens obtained during pregnancy or at delivery, 37 contained a portion of the coexisting corpus luteum. Only 2 corpora were contained in the ovarian specimens from the 6 postpartum patients.

Size.—As shown by others, size varies considerably. A corpus luteum found during pregnancy is usually larger than that accompanying the menstrual cycle. This is especially true during the early part of pregnancy. Size depends a great deal on the capacity of the *centrum* or central cavity. If this is large, the corpus luteum becomes "large," the wall (granulosa and theca lutein layers) being thinned by stretching over the surface to the point of replacement in some areas by a fibrous envelope only (Fig. 1). If the cavity is smaller, the corpus luteum is likewise diminished in size and the wall correspondingly thicker and more convoluted.

The only significance which can be attached to greater size alone is the increased ease with which it allows gross identification. In each instance, at operation, an attempt was made to select the area for biopsy which included a portion of the corpus luteum. There were no failures when the patient was in early pregnancy (Group 1). Out of 25 biopsies in the second group (when the central cavity is smaller or absent), the corpus luteum was missed 10 times.

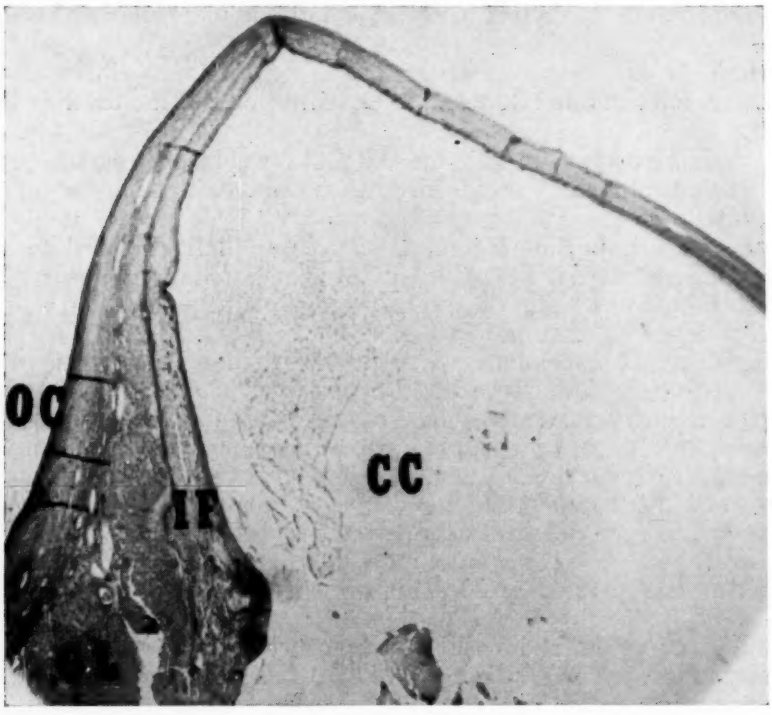


Fig. 1.—Case 8 (132836). An early cystic corpus luteum from a 9 weeks' gestation, showing the gradual thinning of the typical layers of the wall and replacement by a fibrous envelope. *OC*, Ovarian cortex. *CC*, Central cavity. *GL*, Granulosa lutein layer. *IF*, Inner fibrous layer. (Milligan trichrome stain. ×12.)

It may therefore be said that, during the first two thirds of pregnancy, the corpus luteum is frequently larger than that of menstruation and larger than that of the last one third of pregnancy. During the last trimester of pregnancy, the corpus luteum is not a conspicuous structure and often is as small as, or smaller than, the corpus luteum of menstruation.

Cavity and Centrum.—A fluid-filled central cavity was present in all but 3 of the 19 early corpora lutea, but was found in only 6 of 18 term or near-term specimens (Table I). Herein, the size of the cavity was classified "large," "medium," or "small." More exacting measurements are not feasible because of the method used to collect material.

The matter of the size of the cavity and corpus luteum has been considered extensively by others.[15] Table I divides our specimens by the nature of their cavity. Note that no "large" central cavity (and thereby, no "large" corpus luteum) was found after the twenty-eighth week of gestation. Three corpora lutea in Groups 1 and 12 in Group 2 contained no cavity.

The centrum of the early "solid" specimens was filled with a loose, mesenchyme-like connective tissue. This became dense peripherally so as to blend imperceptibly with the inner fibrous layer. No vessels were present.

TABLE I. CAVITY IN CORPUS LUTEUM OF PREGNANCY

	GROUP 1		GROUP 2	
Number of specimens	19		18	
Central cavity present	16		6	
Large		13		0
Medium		2		3
Small		1		3
Central cavity absent	3		12	

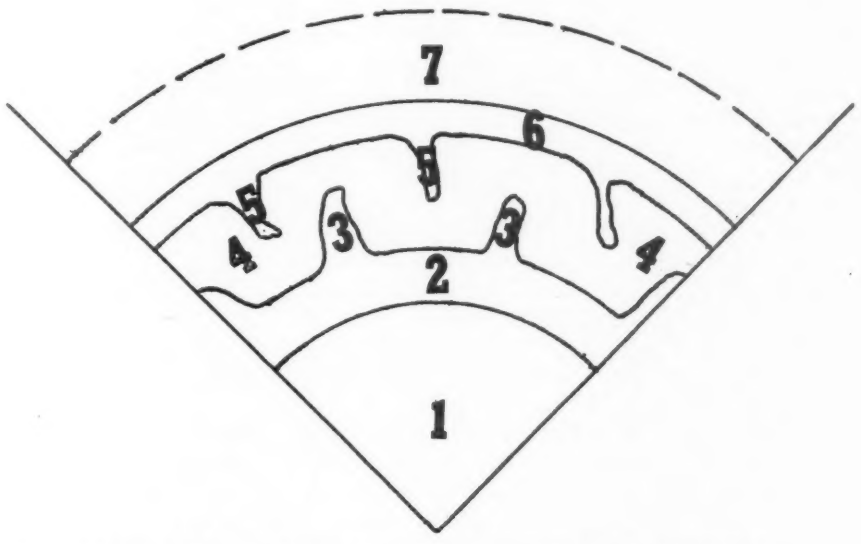


Fig. 2.—Diagram of layers in a segment of a corpus luteum in pregnancy.
1, Central cavity
2, Inner fibrous layer
3, Trabeculae (fibrous)
4, Granulosa lutein layer
5, Trabeculae (theca lutein)
6, Paralutein cells (theca interna)
7, Theca externa

The next older specimen with no central cavity was at 27 weeks' gestation. In it the connective tissue was a fine meshwork of collagenous and reticular fibers. The vessels were large and numerous, filled with blood, and located peripherally within the centrum and within the inner fibrous layer. The centra of older corpora contained heavier connective tissue, which at times was hyalinized. If hyalinization was prominent, as it was in one, the vessels were few and the hyalinized fibers formed a wavy line just within the inner fibrous layer. This colored a deep pink with the eosin and a brilliant green with Milligan's trichrome stain. Heavy reticular fibers were intermingled and particularly dense. Hyalinization of the centrum was found in only 3 term specimens. There was considerable difference in the histological "aging" of various corpora of equal "menstrual age."

Supporting Structures.—The layers of the corpus luteum of pregnancy may be compared to those of a golf ball (see diagram in Fig. 2). An inner shell (fibrous layer) is supported by and derived from a series of many struts (fibrous and theca lutein trabeculae) which arise peripherally from the outer shell or theca externa. The vessels supplying the corpus from the substance of the ovary spread out over this external capsule and branch centrally through

the lutein trabeculae to the centrum or inner fibrous layer. An intricate and elaborate supporting system of reticular fibers can be followed in all these structures as well as in the interval compartments occupied by the granulosa and theca lutein cells.

Inner fibrous layer: As noted, all but 3 of the early corpora had large cystic, central cavities. With these exceptions then, the inner fibrous layer of Group 1 specimens served both as a capsule to the cavity and as the inner lining of the granulosa lutein layer. An inner, one-cell, endothelium-like layer lined each cavity. These cells appeared to be flattened fibroblasts. The inner fibrous layer was composed of fibroblasts, collagen, and reticular fibers, and contained an assortment of blood vessels. Adjacent to the cavity, it was loose and mesenchymal in character but became more dense near the granulosa lutein layer. The collagen fibers seemed to become coarser in older specimens. In some larger corpora, the granulosa lutein layer was narrowed to the width of a few cells. In such areas the inner fibrous layer was wider and the wavy collagenous fibers heavier than elsewhere in the same specimen.

Only 2 specimens contained old clots in the centrum.

Two corpora (16 and 27 weeks of age) had densely organized collagenous fibers with hyalinization. In one, that at 27 weeks, beginning calcification was noted. In both, the outer one third of the layer (nearest the granulosa lutein layer) retained its loose, mesenchymal character.

A mesenchymal core replaced the central cavity in 3 specimens from 7, 8, and 13 weeks of age. In these 3, the inner fibrous layer was indistinguishable from the tissues of the centrum.

Basically, the inner fibrous layer of the Group 2 specimens appeared similar to that described in the foregoing. The layer was less cellular, however, more densely constructed, and contained heavier and more closely packed collagenous fibers. This was particularly true of the inner two thirds of the layer; the outer one third remained mesenchymal. Nine of the 18 specimens showed hyalinization of the inner fibrous layer and a few demonstrated calcium salts.

Trabeculae (fibrous): These triangular palisades of support are similar to the inner fibrous layer in composition. The base abuts the inner fibrous layer and the apex is directed toward the theca externa. They contain no theca lutein cells. Theca lutein trabeculae (see "Theca lutein layer") originate peripherally from the theca interna layer, have apices directed inward toward the inner fibrous layer, and accompany the centripetally growing vascular system.

The corpora in Group 1 showed few and only moderately well-developed fibrous trabeculae. The trabeculae lagged behind their respective inner fibrous layers in development, for they remained more loose and cellular, and with finer collagenous fibers. No hyalinization was found.

In Group 2, the trabeculae were more compactly constructed, had heavier collagen fibers, and in some instances contained areas of hyalinization. When there was hyalinization, it was present in the inner fibrous layer also. No calcium salts were found.

Because of individual variation, these structures cannot be used to predict accurately the age of an individual corpus other than to say it is one of an "early" or "late" pregnancy.

Theca externa: Concerning this layer we are also almost "content to admit its presence and say no more."[15] Its constituents are those of the surrounding ovarian stroma. It is more vascular. One would think it should be compressed by the expanding corpus, but it remains more loosely arranged than the surrounding stroma. Shrinkage in size with age might also mechanically contribute to the increased looseness of this layer, but the "looseness" is no greater in the latter parts of pregnancy than in early pregnancy.

Recticular network: Four Group 1 and two Group 2 specimens were stained for reticular fibers. Varying from fine to coarse and from loose to compact in arrangement, these fibers mimicked the structure of the corpus so as to provide a skeleton upon which its cellular elements rested. The network was most compactly constructed about vessels at the periphery of the inner fibrous layer, in the fibrous trabeculae, and throughout the theca lutein layers. There was no basic difference in the nature of the fibers between the two groups. Fibers tended to become progressively finer as they followed the smallest capillary winding its way between glandular cells.

Fig. 3.

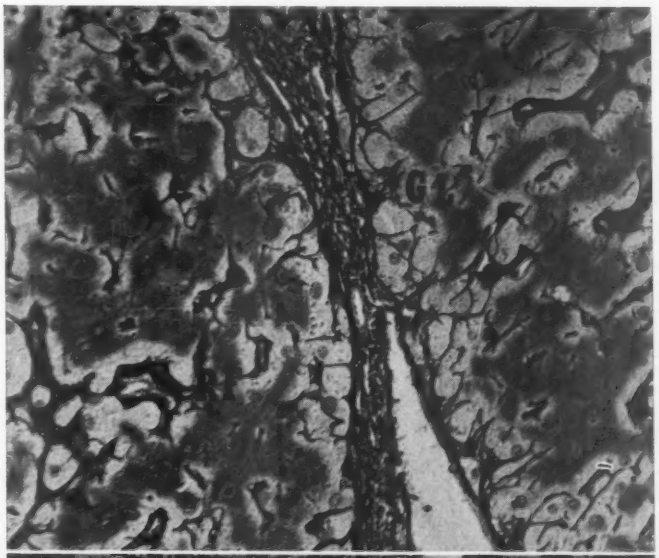


Fig. 4.

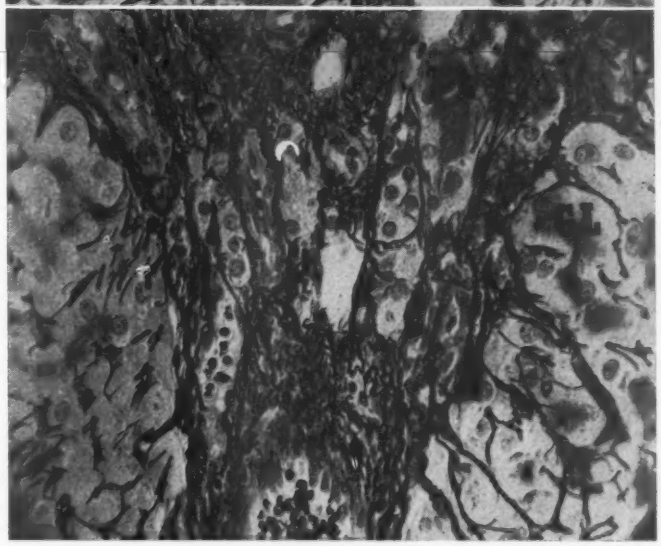


Fig. 3.—Case 39 (322804). A portion of the granulosa lutein layer of the corpus luteum from a term pregnancy, showing distribution of reticular fibers within that layer. *GL*, Granulosa lutein layer. *RF*, Reticular fibers. (Reticulum stain counterstained with hematoxylin and eosin. ×225; reduced ⅙.)

Fig. 4.—The same section as Fig. 3. This area shows in addition the tendency of reticular fibers to surround groups of theca lutein cells. *GL*, Granulosa lutein cells. *TL*, Paralutein (theca lutein) cells. (×437; reduced ⅙.)

In the granulosa lutein layer, reticular fibers were found supporting groups of cells; peripherally and next to the fibrous trabeculae they might surround individual cells (Fig. 3).

In the theca lutein layer, fine fibers supported groups of cells (Fig. 4). As theca lutein cells became less prominent, groups of several tiny, shrunken nuclei might yet be found within the reticular meshes. These findings agreed with those of Gillman and Stein.[6]

Vascular network: Vascularization occurs before fertilization, at a time when it is yet unknown whether a given corpus luteum is to be one of menstruation or of pregnancy. These processes Brewer[2] has aptly described. Following this early stage, further development of vessels is a matter of "growing up." White and associates[23] failed to mention the vascular system of their remarkably early corpora of pregnancy. Other specimens, including our own, are from pregnancies aged 35 days or more. By this time, the vascular systems of the corpus have become well established and stabilized.

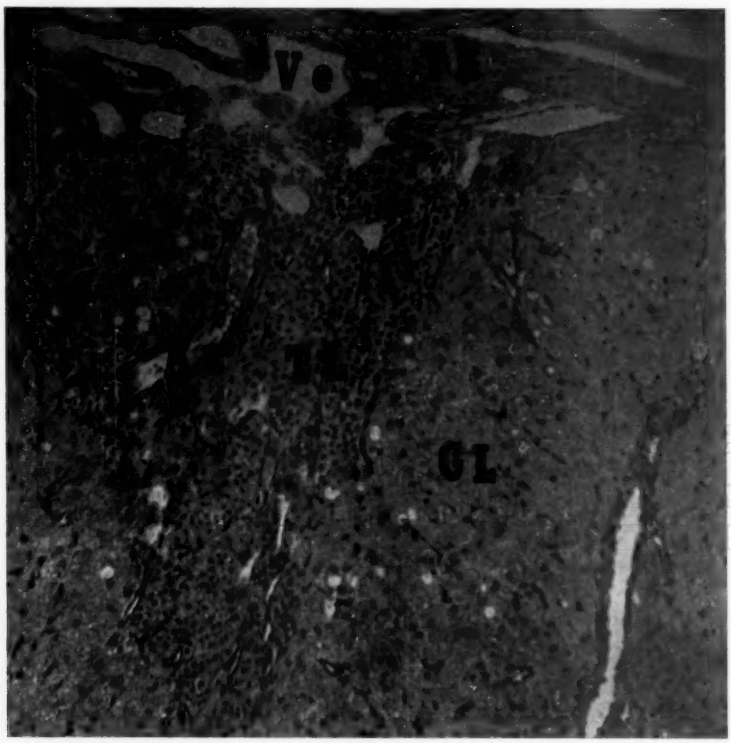


Fig. 5.—Case 3 (335118). An area from the periphery of a corpus luteum from a 6 weeks' gestation, demonstrating the vascularity noted in most early specimens. Numerous venous channels with well-developed arterioles are a prominent finding. *GL*, Granulosa lutein layer. *TL*, Theca lutein cells. *Ar*, Arterioles. *Ve*, Venules. *TE*, Theca externa. (×81.)

Vessels of the ovarian stroma in the area of the developing corpus luteum apparently enlarge and multiply in number commensurately with its new metabolic demands. From the very vascular theca externa next to the ovarian side of the corpus (Fig. 5), vascular channels can be followed inwardly through the theca interna. They traverse the theca lutein trabeculae to spread within the inner fibrous layer over the inner surface of the granulosa lutein layer and extend peripherally again in the fibrous trabeculae. In all our specimens, these main vessels were well developed, showing substantial walls with patent or

dilated lumina, and containing considerable blood. Surrounding connective tissues supplied adequate support, for reticular fibers were especially heavy and compactly placed about these vascular channels. Smaller vessels traversed the theca and granulosa lutein layers accompanied by a minimum of connective tissue. Numerous capillaries noted in the Group 1 and early Group 2 corpora completed the picture. In the granulosa lutein layers, capillaries were numerous, straight, contained blood, and coursed between columns of the luteinized cells. When the corpus became older, some capillaries collapsed and were replaced by reticular and fine collagenous fibers. Those that remained open were supported by heavier and more substantial connective tissue.

Older specimens might also show sclerosis in arterioles of the theca externa, theca lutein, and the trabeculae (Fig. 6). There was a thickening of the media with encroachment upon or complete obliteration of the lumina. Two Group 1 and 8 Group 2 corpora revealed sclerosis of varying degrees.

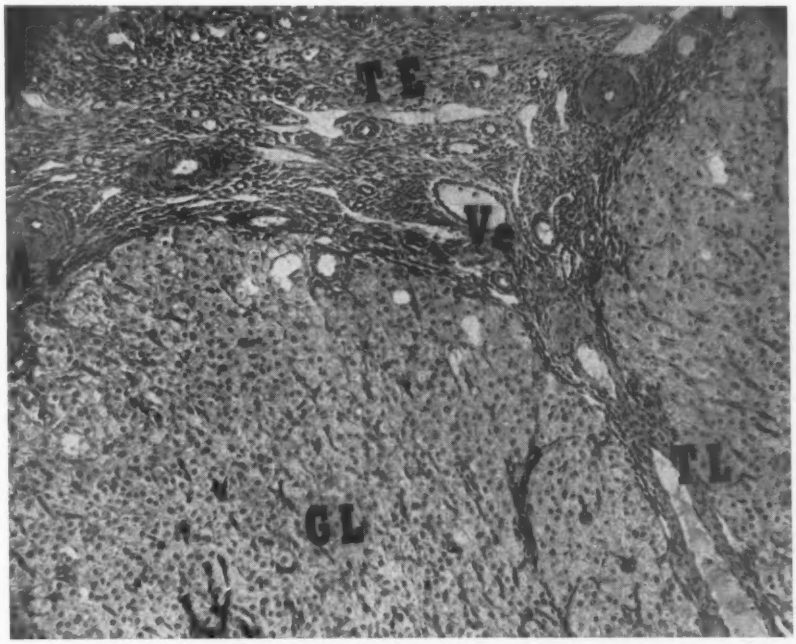


Fig. 6.—Case 42 (281867). A portion of the periphery of a corpus luteum from a term pregnancy which depicts the aging of its vascular network. Arteriolar walls have become thickened at the expense of the lumina. Venules are fewer in number. Few if any distinguishable theca lutein cells remain. *GL*, Granulosa lutein layer. *Ar*, Arterioles. *Ve*, Venules. *TL*, Theca lutein cells. *TE*, Theca externa. (×97.)

Cellular Layers.—These contain the functioning units of the corpus luteum of pregnancy, namely, the epithelioid granulosa and theca lutein cells.

Granulosa lutein layer: Its convoluting form and yellow color first brought attention to the corpus luteum and still permit an immediate identification at the operating or necropsy table (Fig. 2). On cross-sectioning, its undulating course is easily delineated. In the earlier, more cystic corpora, undulations are less marked because the layer becomes "stretched out" to cover the increased surface. In some areas, the layer becomes thinner and may be replaced entirely by connective tissue (Fig. 1). In the young, smaller corpora with a solid central core, undulations are marked. The exterior indentations are filled by the triangular-shaped theca lutein trabeculae; the inner, by fibrous

tissue trabeculae. In older corpora, the granulosa lutein layer becomes more highly organized; for connective tissue elements increase, theca lutein cells are fewer and their trabeculae decrease in numbers, are narrower, and more solid. As a result, undulations are obliterated with the formation of a compact circular shell on cut section. In these specimens and those without a central cavity, the layer is its broadest and most conspicuous. In any event, the granulosa lutein layer is the only constant and ever present feature of corpora lutea of pregnancy or menstruation. Yet its constituents are ever changing and vary with increasing age.

Individual granulosa cells were well luteinized in our first specimen of 5 weeks. Two types of cells could be recognized. The first, and by far the more abundant, was the large, rounded, or polyhedral cell with a homogeneous, pink-staining cytoplasm making up the bulk of the layer. The vesicular nucleus was oval or round, with a thin but distinct nuclear membrane, and one or two prominent nucleoli. The less common second cell type was stellate in shape, had dark, heavier-staining cytoplasm and a shrunken hyperchromatic (but to us pyknotic) nucleus in which details were obscured or absent. These fitted the previous description of "light" and "dark" cells.[6] The "dark" cells have been noted by others in early specimens.[8] They were later dubbed the "K" cell. "K" cells are said to be few in number at 29 days (4 weeks) and after. None were seen after 4 to 4½ months of pregnancy.[23] We found stellate cells of White's description present throughout pregnancy. They were a frequent finding in 9 Group 1 specimens. Their location was primarily in the outer one third, although some cells were usually scattered throughout the granulosa lutein layer. The cell was infrequent in 8 other corpora and not evaluated in the remaining 2 because of autolysis. In our specimens, stellate cells were more numerous from the eighth to the sixteenth week of gestation. Following this time, they were seldom seen, being absent in 10 and only "few" in the other 7 corpora. On the other hand, one corpus, at 39 weeks' gestation, contained an abundant number. We believe these cells resulted from early degenerative changes in individual granulosa lutein cells.

Other cell modifications of the typical granulosa cell are designated "prickle cells."[7, 23] Small, numerous peripheral cytoplasmic vacuolations in adjacent cells make boundaries indefinite and give an appearance not unlike that of the prickle cell in squamous epithelium (Fig. 7). In our specimens they were most common in the inner one third of the granulosa lutein layer of 13 early corpora, none were found in 4 others, and the remaining 2 could not be evaluated again because of autolysis. No "prickle cells" were seen after the sixteenth week of gestation. Their disappearance corresponded to that of the "K" cell described by others.[23]

We took no exact measurements of the size of granulosa lutein cells. In the early specimens, they were larger and more plump than in the Group 2 corpora. Cellular outlines were not as distinct, and the arrangement was less compact in Group 1 specimens. Cellular borders became more distinct, the cells smaller, and the layer more compactly arranged in older corpora. These changes could in a large measure be attributed to the disappearance of fine vacuoles as corpora became older. It was after the sixteenth week that this relative absence of vacuoles helped produce a more compact appearance in the granulosa lutein layer.

Pyknotic nuclei were abundant throughout the granulosa lutein layers of 6 Group 1 and 2 Group 2 corpora lutea. Transition forms from shrunken or wrinkled nuclear membranes to full-blown pyknosis could be seen in all corpora from Group 1. Shrunken and wrinkled nuclei were seen frequently in Group 2 corpora even though pyknosis was scarcely found. Vacuolated or

stellate cells in the granulosa lutein layer also contained the pyknotic nuclei. Corpora containing such cells were almost entirely limited to the first group of specimens except for the 2 term corpora, which also showed stellate and vacuolated cells. On the other hand, earlier nuclear degenerative changes—wrinkled, shrunken nuclear membranes—were prominent in older corpora.

Theca lutein layer: Immediately adjacent to the granulosa layer, some authors have described a "basement membrane" between the granulosa and theca lutein layers. No such structure was demonstrated in any of our specimens. By the special stains, however, a condensation of reticular fibers at the periphery of the granulosa layer could be seen in most corpora.

Surrounding the granulosa lutein layer of early corpora was a layer of luteinized theca cells. These arose from the theca interna layer and were typically well developed in our earliest specimen. The individual cell was a small, polyhedral, or rounded cell with a darker-staining, more granular cytoplasm than was seen in granulosa lutein cells. The nucleus was centrally placed, round, and more chromatic than that of the granulosa. One or two prominent nucleoli were usully present. In size, they were about one fourth the diameter of a granulosa lutein cell.

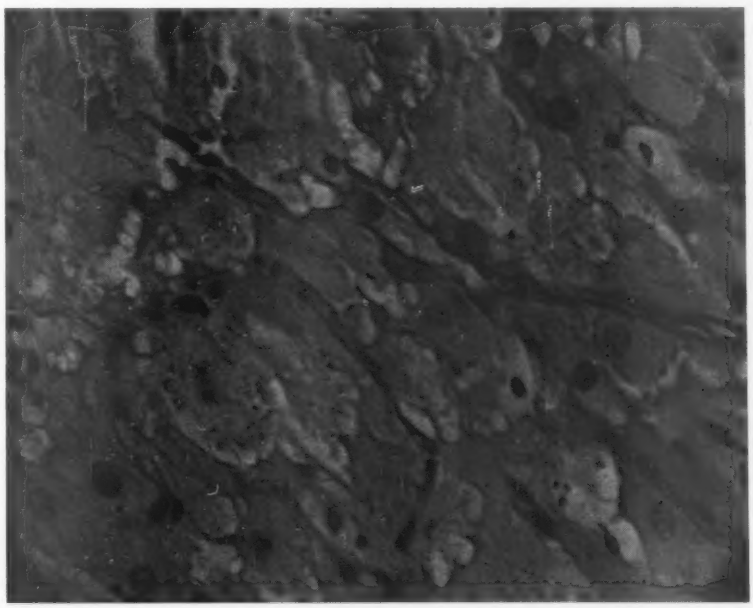


Fig. 7.—Case 1 (315512). Peripheral vacuoles of adjacent granulosa cells in a corpus luteum from a gestation of 5 weeks suggest the designation of "prickle cells," sometimes seen as a modification of the granulosa lutein cells in corpora of early pregnancy. (×375.)

Theca lutein cells ensheathed blood vessels as they penetrated the space between the festoons of the undulating granulosa lutein layer. On cross section, the theca layer therefore became triangular shaped with the base placed peripherally and the apex centrally (Figs. 2 and 5). Sometimes the only theca lutein cells in evidence were cut off from the periphery, forming islands surrounding the vessels and engulfed within the granulosa lutein layer.

Only 3 corpora contained no theca lutein cells (Table II). These were all from pregnancies at or near term. In one, there was moderate autolysis. In another, innumerable shrunken nuclei without discernible surrounding cytoplasm were found in the regions ordinarily occupied by the theca lutein cells; in the third, they were just absent.

TABLE II. THECA LUTEIN REACTION IN CORPORA LUTEA OF PREGNANCY

	GROUP 1	GROUP 2
Number of specimens	19	18
Type of reaction		
Marked	15	0
Moderate	3*	6
Slight	1†	9
Absent	0	3‡

*Case 6, 8 weeks. Case 10, 10 weeks. Case 11, 12 weeks.
†Case 15, 27 weeks.
‡Case 19, 37 weeks. Cases 32 and 42, both 40 weeks.

Corpora from the first months of pregnancy showed exuberant growth of theca lutein cells, while those from the last 2 months contained few. Except in one instance, no "flourish" of these cells was found in the last month of pregnancy as is maintained by Pratt.[20] Neither were they absent after the fifth month, as is said to be true by the majority of authors.[15] Relationships to theca lutein reactions throughout the remainder of ovarian structures as considered by Papanicolaou[18] will be discussed later.

In some early corpora, transition forms from fibroblasts to luteinized theca cells could be seen. The reverse process seemed to be present in the older corpora, but this may have been an observational artifact. Theca lutein cells apparently originate in situ from fibroblastic cells which surround the blood vessels of the theca interna. Such vessels carry blood with the highest concentration of hormone substances. Cells immediately surrounding the smaller of them would logically be exposed to the greatest hormonal influence and be most apt to be affected by it. One of us (R. R. G.) was impressed also by possible transition forms between theca and granulosa lutein cells found in 3 corpora.

Theca lutein cells were abundant at the periphery of 15 out of 19 early corpora. When so placed, they are called "paralutein" cells.[19] In the remaining 4 corpora, "paralutein" cells were few in number. In 2 of these latter specimens, theca-cell trabeculae were well developed. In the remaining 2, only few theca lutein cells were found.

As previously stated, in 3 corpora from the second group, no theca lutein cells were found even after additional sections were examined. In addition, "paralutein" cells were absent from 4, "few" in 5, found only at the base of theca-cell trabeculae in 3, and abundant in the remaining 3. Only one corpus contained "paralutein" cells without theca lutein trabeculae. Seven of the 14 with good theca lutein trabeculae also had fusiform transition forms. Stages of transition from flourishing theca lutein cells to cells with indefinite cytoplasmic boundaries and long, thin, dark-staining nuclei were seen. These were much like cellular elements which made up the general ovarian stroma.

Although pyknosis could be found in most all corpora of both groups, it was not a prominent finding in this layer.

Acinar arrangement of thecal cells was found commonly. In such groups, 5 or 6 healthy cells were arranged together. Such rosettes were suggestive of Call-Exner bodies in growing Graafian follicles. The central space, if present, however, did not contain a dark-staining, colloidlike substance.

Glandular-cell inclusions: Six cellular inclusions have been described within granulosa or theca lutein cells of the corpus luteum of pregnancy. They are: (1) secretory granules, (2) lipids, (3) colloid, (4) vacuoles, (5) chromidial substance, and (6) mitochondria or Golgi apparatus. No attempt was made to study the last two. We believe all others may be found in either granulosa or theca lutein cells, whereas Gillman and Stein,[6] who considered these substances thoroughly, denied finding colloid or vacuoles in theca lutein cells.

(1) Secretory granules: A search for secretory granules as described by Gillman and Stein was made in 4 corpora of Group 1. The granules are brought out best by focusing up and down under oil immersion. Will Milligan's trichrome stain, erythrocytes, colloid material, and the secretory granules stain a brilliant, almost irridescent red. In all 4 corpora, there were irregular-shaped, granular substances within some (though less than 50 per cent) of the granulosa and theca lutein cells which fitted the description given by the former authors for their "secretory granules." These granules were of all sizes and shapes. Some became large and characteristic enough to be indistinguishable from "colloid" which was often present within the same granulosa cell. Smaller "secretory" droplets of the same nature could also be found in some theca lutein cells (compare with Fig. 9).

They appeared to us like granular cytoplasmic debris. Our belief is strengthened by their similar staining to and association with the colloid material—a degenerative product. We suggest that these "so-called secretory granules" may well be precursors of colloid material.

Outside the possible relation to colloid described in the foregoing, we are unable to connect the granules with the vacuoles. Gillman and Stein[6] described them in cells which have only small vacuoles. Their absence in cells which contain the large degenerative vacuoles may be explained simply by the fact that such spaces leave little or no cytoplasm in which anything at all can be found. We feel that if there is any significance to this relationship it is probably just as simple as that.

(2) Lipids: In the first group of corpora, tiny fat droplets were scattered diffusely throughout the cytoplasm of most of the granulosa lutein cells. The droplets were usually fewer and larger in the more central lutein cells, and finer and more abundant in those of the periphery. Considerable variance from one area to another of the same specimen was noted. In general, the younger the corpus, the more abundant the lipoid material. In the 4 term or near-term corpora, the globules were scarce, scattered, and large. The theca lutein layer of the 3 corpora could not be distinguished. In the others, droplets were generally larger and fewer than in the granulosa lutein cells.

(3) Colloid: For purposes of identification of a corpus luteum of pregnancy, this is the most important single intracellular inclusion. It is intimately related to calcium which will be considered with it. Table III gives the distribution of these substances.

TABLE III. COLLOID AND CALCIUM IN CORPORA LUTEA OF PREGNANCY

	GROUP 1		GROUP 2	
Number of specimens	19		18	
Colloid				
Present	19		16	
Abundant		8		0
Moderate		5		2
Little		6		14
Absent	0		2*	
Calcium				
Present	0		13	
Abundant				2
Moderate				1
Little				10
Absent			5	

*Cases 32 and 34 (both 40 weeks): No colloid but calcium present.

Colloid and/or calcium are the most consistently found inclusions within the granulosa lutein cells of the corpus luteum of pregnancy. Either one or the other is found in every corpus, colloid being by far the most abundant. Only 2 corpora lutea did not contain some colloid. Both failed to contain colloid material in 5 additional sections studied in a special effort to find it. Both were from term pregnancies. One was not well-fixed tissue, showing considerable autolysis, which makes finer histological evaluation of any sort hazardous. In both a rare calcium globule was detected.

All the specimens of Group 1 corpora contained colloid, although the amount in each was variable. No definite relationship with the amount present and the duration of pregnancy could be established but the 6 specimens from the seventh to the tenth week of gestation all contained an abundant amount. Calcium was not found in any of the Group 1 corpora.

Sixteen of the Group 2 specimens showed colloid. The majority contained only a small amount and 2 a moderate amount. It was not found abundantly in any of this group. Thirteen showed calcium deposits, most usually in small amounts.

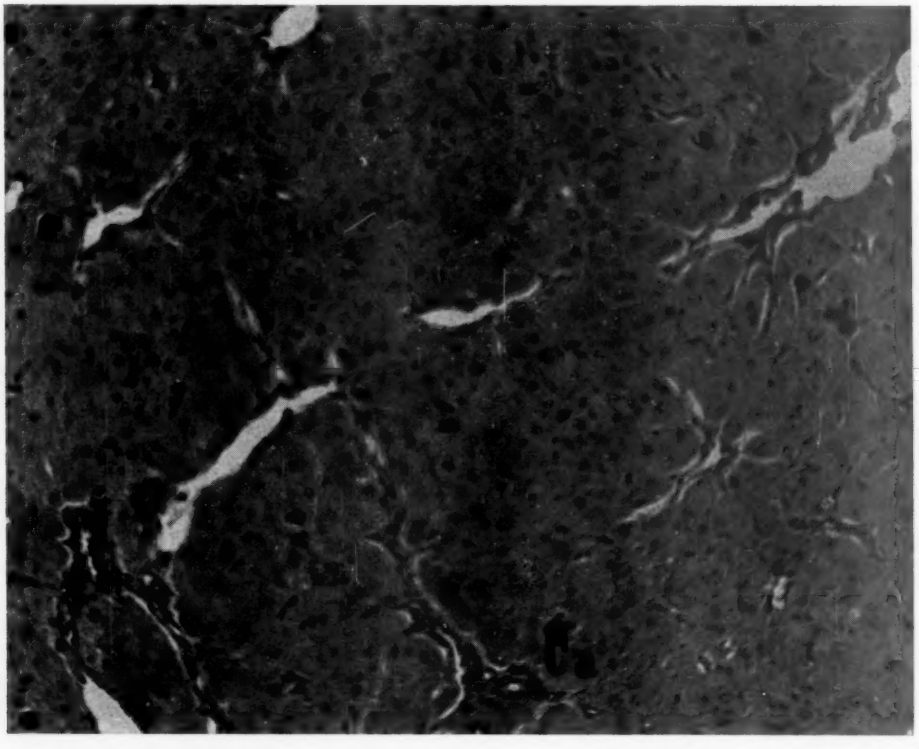


Fig. 8.—Case 25 (332387). An area in a granulosa lutein layer from a corpus luteum of 38 weeks' gestation, to demonstrate the scattered purple-staining globules thought to be calcium. *Ca*, Calcium. (×150.)

All imaginable shapes and sizes of colloid particles could be found. Usually circular or crescent shaped, droplets ranged in size from that of an erythrocyte to irregular globules taking up most of an entire granulosa lutein cell. The material stained from a delicate pink to a brilliant red with the methods employed. The larger the globules, the greater was the tendency to take on also a purplish hue. All shades of color from pink colloid to the deep purple calcified globule were frequently present in the same corpus. Conglomerates

of tiny red droplets sometimes appeared to be in the process of forming larger droplets. Their relationship to the so-called "secretory granules" has been previously mentioned.

Innumerable forms of colloid globules were also seen in conjunction with vacuoles of degeneration. With the decrease in numbers of vacuoles in the Group 2 corpora, colloid also became less in amount. It might require searching, occasionally in several sections, before it could be found.

On the other hand, older corpora revealed large, irregular-shaped, deep-purple-staining globules presumed to be calcium. Although the globules were usually few in numbers, 2 term specimens contained an abundance. The shape and general appearance of a calcified globule could best be described as the microscopic counterpart of a "clinker" (Fig. 8). They often seemed closely related to colloid and/or vacuoles. Sometimes a portion of a large, red-stained colloid globule appeared calcified. Gillman and Stein[6] have best illustrated these relationships by their "formula":

$$\text{Vacuoles} \rightleftharpoons \text{Colloid} \rightarrow \text{Calcium.}$$

It is probable that calcium is later absorbed, by what process we do not know, for it is not a finding in corpora albicantia, the "skeletal remains" of all corpora lutea. We do not know, however, that we have examined many (if any) corpora albicantia that resulted from regression of a corpus luteum of pregnancy.

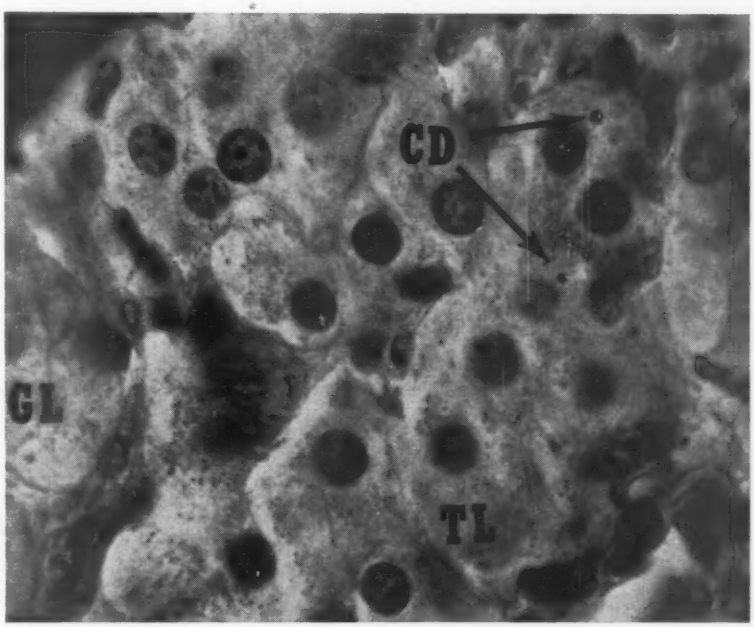


Fig. 9.—Case 39 (322804). Theca lutein cells at the periphery of the granulosa lutein layer—paralutein cells of Fintо—from a corpus luteum of term pregnancy, which we believe contain small colloid droplets. *GL*, Granulosa lutein cells. *TL*, Theca lutein cells. *CD*, Colloid droplets. (Periodic acid stain. ×1,260.)

Colloid or calcium is not selectively distributed to any particular zone of the granulosa lutein layer. Sometimes more colloid seems to be found in the outer one third. Usually, though, these products are scattered erratically throughout.

The close relationship of colloid to degenerative vacuoles leaves little doubt in our minds that it represents, with few exceptions, the result of a

special degenerative process in the granulosa lutein cell. This belief is strengthened also by its attraction for calcium and its accompaniment by cytoplasmic cellular debris and nuclear pyknosis. All of these are evidences of cellular degeneration. Although at times seen in stellate cells, there is no evidence that it must always and only be harbored in this type of cell. Conversely, colloid is rarely present in the corpus of menstruation, even though stellate cells may be plentifully found.[2, 15]

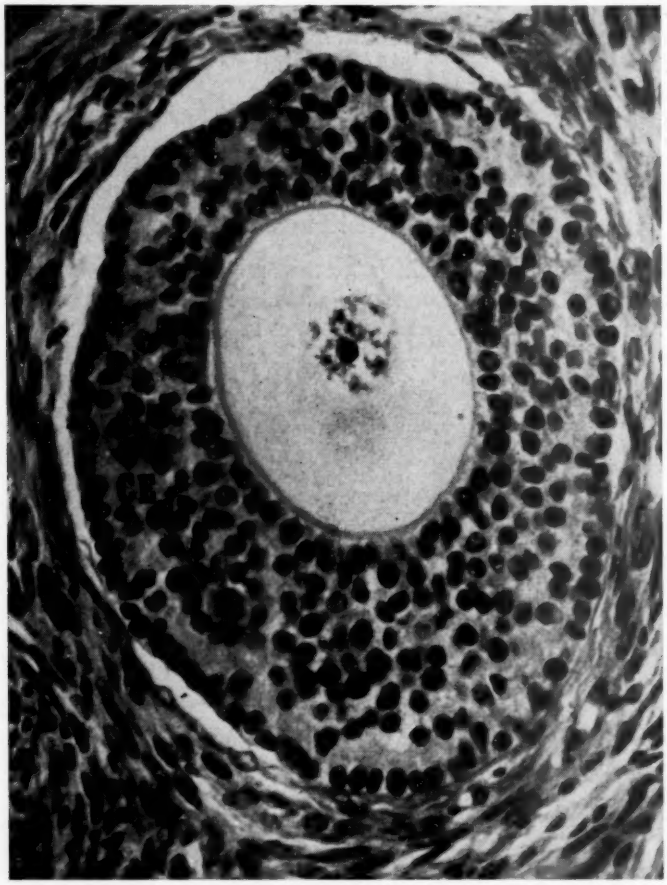


Fig. 10.—Case 10 (318158). A very early developing follicle in the ovary from a 10 weeks' gestation, which contains two Call-Exner bodies surrounded by granulosa cells. Such "bodies" have staining qualities identical with the colloid seen in the granulosa lutein layers of corpora lutea of pregnancy. *CE*, Call-Exner body. (×600; reduced ¼.)

Although it is denied by other authors, we are both impressed with the possibility that colloid may also occasionally be present in theca lutein cells (Fig. 9). We believe colloid was seen in the theca lutein layer of 4 corpora. At least, a substance with the staining qualities and the shape of colloid material was present. It may just be possible that secretory granules had coalesced to form a larger droplet. Which of the two is the case cannot be determined with absolute certainty.

Ironically, after convincing evidence that colloid is a degenerative product which appears only following aging of the corpus luteum in pregnancy, it was noted to have staining properties similar to those of the Call-Exner bodies in the granulosa layer of early developing follicles (Fig. 10). Could not these

substances be identical, even though no "K" cells, "dark" cells, or luteinized granulosa cells were found in this structure? Although most authors have denied that colloid occurs in a menstrual corpus luteum, its presence here has also been described.[13] On rare occasions, therefore, colloid material may be demonstrated in any ovarian structure.

(4) Vacuoles: Empty spaces left by fallen-out or washed-out products of cellular metabolism or degeneration are designated "vacuoles." Two types are to be considered.

The first kind are regarded as evidence of secretory activity. They are best demonstrated in the early corpora of Group 1. These vacuoles were small and occupied the periphery of the cell, so that, when observed in adjacent cells, a "prickle cell" appearance resulted. They have been described by others[7, 23] in the early corpora of pregnancy. They were fairly prominent within the inner one third of the granulosa lutein layer of 8 out of 11 of our corpora through the eighth week of gestation. Such vacuoles were a feature of all but 6 specimens from Group 1. None were seen in the second group.

The other type of vacuoles found throughout pregnancy accompany degenerative changes. The vacuoles were also most frequent in Group 1 specimens, occupied cells that had a pyknotic or shrunken nucleus, and occurred in greatest numbers when present with colloid. At such times they assumed all imaginable shapes, sizes, and relationships to that material. The vacuoles were prominent in 15 of the Group 1 specimens, while only few were present in most corpora of the second group. There was no predilection for a particular area of the granulosa layer. If there were more "prickle cells," the cells containing degenerative vacuoles occupied the periphery of the layer. Term or near-term specimens usually contained but few degenerative and no secretory vacuoles.

No one has described vacuoles in theca lutein cells. These cells are also actively secreting and should contain vacuoles. We found small theca lutein vacuoles in only 6 of the earliest corpora. There were only a few within each cell, and only a few cells contained them, so searching was necessary. Gillman and Stein[6] denied their presence but inadvertently reproduced similar vacuoles in a photomicrograph of theca lutein cells while illustrating their "secretory granules" (see their Fig. 8).

Postpartum Corpora Lutea.—

Two corpora lutea removed 8 days post partum are available. Both were small and without a cavity. Dense connective tissue central cores were present. Connective tissue was well developed and extensive throughout. Hyalinization was present in the central cores and trabeculae. Arterioles were thick walled, large, opened, and filled with blood. The granulosa cells were small, shrunken, and wrinkled in outline, indicating obvious degeneration. Vacuoles were few, scattered, related to colloid, and degenerative in type. The reticular network remained unchanged. Nuclei because shrunken or pyknotic. The granulosa lutein layer contained many fibroblasts surrounding the degenerating glandular cells. Scattered leukocytes were also moderately prominent. Small amounts of colloid were present in the one and calcium in a like quantity in the other. A theca lutein layer could not be identified in either. Both might be described as degenerating, atrophying, and organizing corpora lutea.

Corpora Lutea of Ectopic Pregnancy.—

In the 24 ovarian specimens from our files which accompanied ectopic pregnancies, thirteen included the corpus luteum. These corpora resembled those of intrauterine pregnancies. An increased number of "dark cells" and cells containing other regressive or degenerative changes was demonstrable in

most of them. This was to be expected, since the death of the products of conception in such patients has usually occurred prior to surgical intervention. If the pregnancies (or trophoblastic elements) remain viable, the accompanying corpus appears as that of any other uterine pregnancy of comparable age (as is seen with an unruptured tubal pregnancy). Calcium is entirely absent. Colloid was present in 10, and again aids in identifying them as coexisting with pregnancy. In 2 of the 3 in which colloid was lacking, accompanying tissue contained no fetal or trophoblastic elements. With the third, trophoblastic elements could be found, for the pregnancy was an unruptured tubal gestation with a macerated 2.0 cm. fetus. Although theca lutein cells were present, the layer was not usually as well developed as in corpora with intrauterine pregnancies of comparable duration.

"Corpus Luteum Cysts."—

Our interest in such cysts stems from being "hard put" to identify a given specimen as one of "pregnancy," of "menstruation," or of a "cystic corpus luteum." In this distinction, colloid plays an important role. In 48 cystic corpora lutea from our files which were suitable for histological examination, colloid was present in 5. Four of these were proved to have accompanied normal intrauterine pregnancy, and were subsequently added to our specimens already discussed. The one remaining corpus contained a minimal amount of colloid. All doubt of a coexisting pregnancy was removed, for the patient had undergone a vaginal hysterectomy and plastic repair. A "cystic ovary" was an incidental finding, and its removal was effected at that time. Therefore, of 45 "corpus luteum cysts," not in any way related to pregnancy, one, or 2.2 per cent, contained a minimal amount of colloid material. It seems probable then that the presence of colloid should permit one to be fairly (but not completely) certain that a pregnancy was also present.

Response of Other Ovarian Structures to Pregnancy.—

The material for this discussion is limited to the study of the 56 ovaries from intrauterine pregnancies, 6 of which are postpartum specimens.

Primordial Follicles.—The ages of the 56 patients ranged from 18 to 42 years and remains unknown in only one. All but 4 specimens, or 52 in number, contained varying numbers of primordial follicles. In the 4 from which these were absent, only a portion of the wall of a cystic corpus luteum of pregnancy was available for study. But for this, it is felt certain that primordial follicles could have been found in all specimens had an adequate area of the surrounding ovarian cortex been also present. None of the primordial follicles showed any changes peculiar to the coexisting pregnancy.

Maturing or Developing Follicles.—That continuation of follicular development extends throughout pregnancy is manifested by the finding of developing follicles in about one half of the ovarian specimens examined. A maturing or developing follicle in pregnancy is identical with that in any ovary with the exception of the additional theca lutein reaction which will be considered below. In some of the early developing follicles, the ovum was also present within the section. Mitotic figures in the granulosa and theca layers are found in these developing follicles. The absence of degeneration, chromatolysis, desquamation, or dissolution of the granulosal elements aids in distinguishing an older, cavity-containing developing follicle from a cystic atretic follicle. Maturing follicles were found in 7 of the 19 from Group 1, in 17 of the 31 from Group 2, and in 4 of the 6 postpartum ovaries.

No basement membrane between granulosa and theca layers is demonstrable other than in primordial or very early developing follicles. As mentioned previously, however, a condensation of the reticular fibers at the periphery of the membrana granulosa is frequently seen when special stains are employed.

Atresia Folliculi.—This process has been adequately described by others and summarized previously. The changes which occur in the doomed follicle have been amply considered.[15, 16, 20, 22] Both the cystic and obliterative atresia as described by Seitz[22] were found in our specimens. Atretic follicles are seen in 11 of the 19 from Group 1, in 27 of the 31 from Group 2, and in all of the 6 from the postpartum period. It is histologically apropos to distinguish (1) an early atretic follicle with all its various stages of cystic or obliterative atresia, from (2) an old atretic follicle, usually called a corpus atreticum or corpus fibrosum. Table IV discloses that an equal number of ovarian specimens contain one or the other or both types of atretic follicle. Had more material been examined from each patient, these structures could most likely have been found in all. The failure to find them seems best explained by the method used in sampling material. We wish to emphasize that, except for the luteinization which occurs with pregnancy, these structures are the same whether from the ovaries of the pregnant patient or of the nonpregnant.

TABLE IV. NUMBER OF OVARIAN SPECIMENS FROM INTRAUTERINE PREGNANCIES WHICH CONTAIN ONE OR MORE OF THE EARLY OR OLD ATRETIC FOLLICLES

	GROUP 1	GROUP 2	POSTPARTUM
Total number of specimens	19	31	6
Number of specimens with			
Early atretic follicles	7	22	5
Old atretic follicles	8	27	6

TABLE V. THECA LUTEIN REACTION IN MATURING AND ATRETIC FOLLICLES

	GROUP 1		GROUP 2		POSTPARTUM	
Total number of specimens	19		31		6	
Number with maturing follicles	7		17		4	
Theca lutein reaction:						
Present	5		17		3	
Marked		0		2		0
Moderate		2		6		3
Slight		1		9		0
Questionable		2		0		0
Absent	2		0		1	
Number with atretic follicles	11		27		6	
Theca lutein reaction:						
Present	5		25		5	
Marked		1		18		4
Moderate		4		5		1
Slight		0		2		0
Absent	6		2		1	

Theca lutein and granulosa lutein reactions in maturing and atretic follicles during intrauterine pregnancy: Luteinization of theca cells, a theca lutein reaction, is found in both maturing and atretic follicles during pregnancy (Table V). In appearance, these cells are identical with their counterparts in the corpus luteum of pregnancy. Such a theca lutein reaction was present in about the same percentage of specimens and to about the same degree in either the maturing or atretic follicles of the Group 1 ovaries. During early pregnancy, the development of the luteinized theca cells in maturing follicles was only moderate in degree. It was absent in 2 out of the 7 specimens which

contained maturing follicles. In atretic follicles, on the other hand, the extent of the reaction was similar, but half of the ovaries examined with atretic follicles present in the section failed to show a luteinizing reaction of the thecal cells.

The theca lutein reaction was found in all but a few maturing and atretic follicles of Group 2 specimens (Figs. 11 and 12). The degree of the reaction was much more intensively developed in the atretic follicles of this group. The reaction was not always of equal development (or intensity) in the maturing or atretic follicles of the same ovary. Apparently older atretic follicles exhibit the most extensive reaction. As pregnancy progresses, the theca lutein reaction of the maturing and atretic follicles gradually increases to become most marked at or near term. Little or no reaction, however, may be seen in some follicles of ovaries in which other similar-sized follicles show a marked theca lutein reaction.

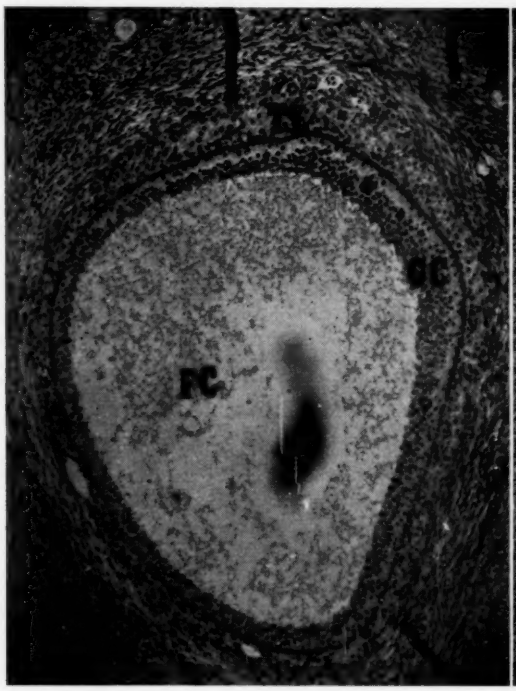


Fig. 11.

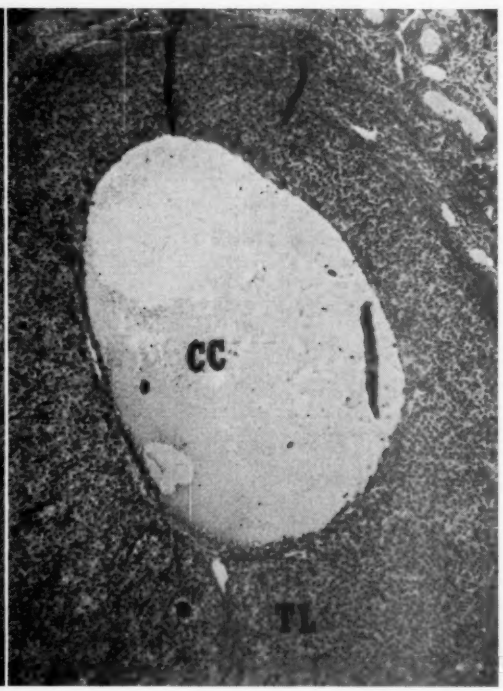


Fig. 12.

Fig. 11.—Case 39 (322804). A maturing follicle from the ovary of a term pregnancy which is surrounded by a well-developed layer of luteinized theca interna cells. The egg was not caught in section, but the granulosa layer contains cells in active mitosis, although not apparent in this photomicrograph. *GC*, Granulosa cells. *TL*, Theca lutein cells. *FC*, Follicular cavity. (×106; reduced ¼.)

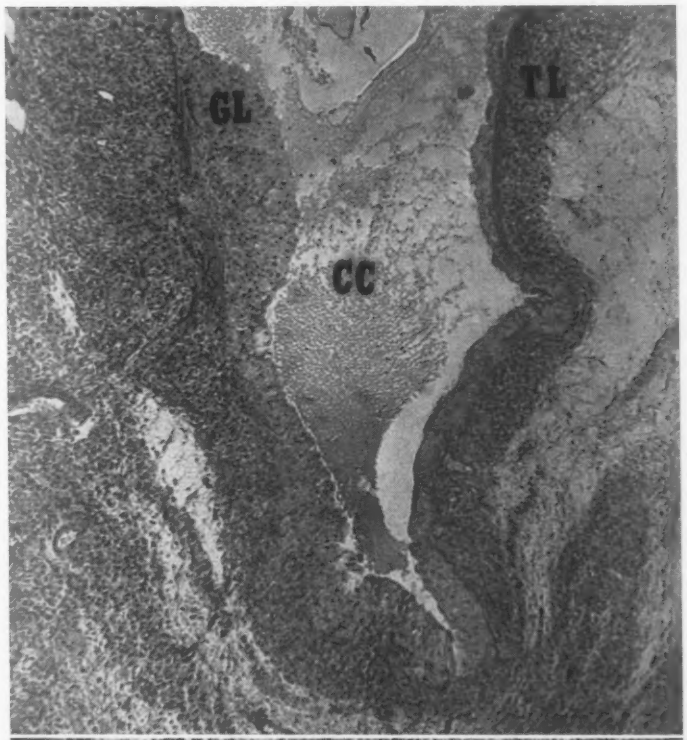
Fig. 12.—Case 39 (322804). A cystic atretic follicle, from another area of the same ovary as in Fig. 11, showing a marked theca lutein reaction. It can be noted that the cavity is lined with a layer of flat, endothelium-like cells which in other follicles seem to round up and become granulosal elements (compare with Fig. 14). *CC*, Central cavity. *TL*, Theca lutein cells. (×80; reduced ¼.)

The reticular network in follicles with a well-developed theca lutein reaction was extensively developed. Fibers tended to surround individual thecal cells in contrast to the thecal and granulosal areas of the corpus luteum.

Although theca lutein elements were present in either maturing or atretic follicles of postpartum ovaries, most of the individual cells appeared degenerative or regressing.

A luteinizing reaction was present in retained granulosal elements of some atretic follicles (Fig. 13). When present, it was always accompanied by a well-developed theca lutein reaction within the same follicle. Transitional stages

Fig. 13.



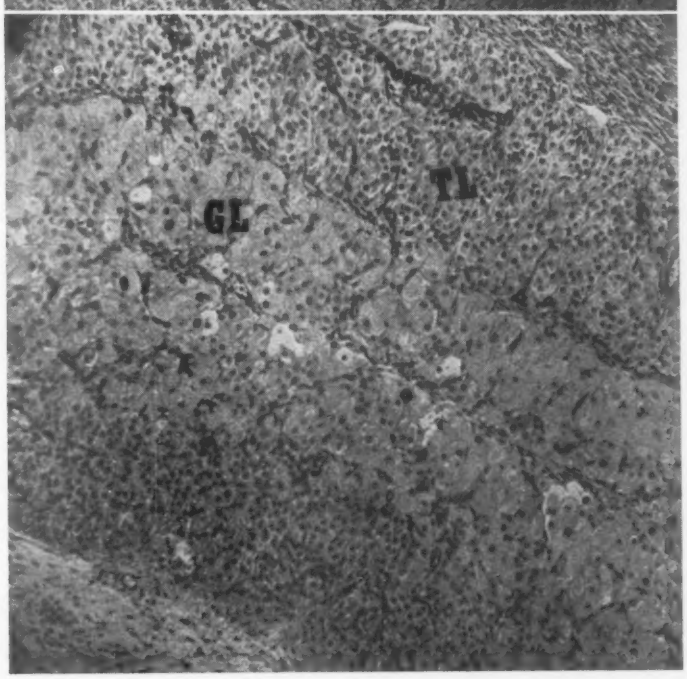


Fig. 14.

Fig. 13.—Case 40 (332001). A cystic atretic follicle from an ovary of a term pregnancy with both marked granulosa and theca lutein reactions. *GL*, Granulosa lutein cells. *TL*, Theca lutein cells. *CC*, Central cavity. (×82; reduced ⅙.)

Fig. 14.—Case 39 (322804). An old atretic follicle from an ovary of a term pregnancy which has both granulosa and theca lutein reactions. No hyaline membrane is yet present. *GL*, Granulosa lutein cells. *TL*, Theca lutein cells. (×125; reduced ⅙.)

from a flat epithelial (endothelium-like) cell lining the cavity of a cystic atretic follicle to a fully luteinized granulosa cell were commonly found. Remnants of the membrana granulosa without reaction were also found in other follicles. In some of these, the inactive granulosa cells were arranged in an alveolar manner although no true Call-Exner bodies were seen. In older atretic follicles (Fig. 14), both luteinized and nonluteinized granulosa cells could be found lying within the interstices of the once prominent hyaline membrane of this structure.

Although the egg was seldom caught in sectioning an early atretic follicle, when seen in a few, it was in good histological condition despite evidences of deterioration of the membrana granulosa. As would be expected, no ova were found in follicles with more advanced atretic changes.

Only isolated examples of corpora albicantia were found. No change attributable to pregnancy was demonstrated within them.

Decidual Reaction.—The appearance of the epithelioid, decidua-like cells within the ovarian cortex during pregnancy has been amply described and portrayed.[5, 15]

A decidual reaction was found in 27 of the 50 ovarian specimens removed during pregnancy and in 4 of the 6 from postpartum patients. The reaction was infrequently observed in early pregnancy, being found in only 4 ovaries from Group 1 patients. On the other hand, a decidual reaction was present in 23 of the 31 from those of Group 2. An additional 3 included areas of endometriosis in which a decidual reaction was well developed. Therefore, only 7 ovaries after the twenty-eighth week of gestation had no decidual reaction. No direct correlation was shown between the extent or amount of a decidual reaction and the duration of the pregnancy. The 4 specimens from early pregnancy contained only a "slight" reaction. In later pregnancy, the reaction was most often judged "moderate" or "marked." Scattered at irregular intervals, however, specimens with "slight" or no reaction were still observed. Reticular fibers encompassed individual cells.

Degenerative changes were found in the areas of decidual reaction from the postpartum ovaries after the seventh day. Specimens within the first 24 hours showed good reactions without deteriorating changes.

In summary, a decidual reaction is difficult to find during the first two thirds of pregnancy. When and if present, it is minimal in extent. In the latter one third of pregnancy, a decidual reaction of considerable extent is present in almost every ovary. Israel and his co-workers[9] observed it in 19 of their 21 term or near-term specimens. We feel, as did Scott,[21] that if material is adequately sampled and sectioned, a decidual reaction could be found in all ovaries from term or near-term pregnancies.

Although of very infrequent occurrence, a good decidual reaction has been seen by us[5] in ovaries from 5 nonpregnant patients.

Germinal Epithelium.—Israel and associates[9] called attention to a change of the germinal epithelium which they felt attended pregnancy, it having been present in 16 out of their 21 term or near-term specimens. Table VI summarizes the results of similar observations in our 56 specimens.

The germinal epithelium is easily destroyed by the handling necessary to obtain and prepare material. Even though care was exercised when the ovary was subjected to biopsy, no more than two thirds of the external ovarian cortex contained intact germinal epithelium in any one specimen. If present, it was found in the depressions of the normally wrinkled and irregular ovarian surface. Characteristically, the cells were either flat or cuboidal in shape. If absent, it was typically missing from the elevated regions, among which localized areas of decidual reaction were noteworthily included.

If labeled as "unchanged," the germinal epithelial cell was flat or cuboidal in shape. If "slightly modified," columnar epithelium with or without peg-shaped cells could be found. When "moderately modified," these changes with the addition of "pseudostratification" were observed. As seen in Table VI, our specimens did not show much alteration in the germinal epithelium. What was present was seen only in isolated areas over the surface. Therefore, on these ovaries which showed some variation, the surface cells were of all described types as one passed over the cortex. Since the changes were so erratic and scattered, we are not at all certain they are characteristic of pregnancy; in addition, neither we nor Israel compared the findings during pregnancy with those from a similar group of nonpregnant patients.

TABLE VI. CHARACTERISTICS OF GERMINAL EPITHELIUM IN OVARIES FROM INTRAUTERINE PREGNANCY

	GROUP 1	GROUP 2	POSTPARTUM
Total number of specimens	19	31	6
Germinal epithelium			
Unchanged	13	16	3
Modified	1	12	2
Slightly	1	9	2
Moderately	0	3	0
Absent	5	3	1

Although others[9] have not found germinal epithelium "recognizable above areas of extensive collection of decidua-like cells," we were able to trace it in several specimens under such circumstances. When present over any raised area, the germinal epithelium becomes flattened—a normal and usual finding. Near and over the surface of the decidual areas it remains unchanged.

Comment and Summary

The reader is referred again to our summary of findings in corpora lutea during the first 30 days of (menstrual) age which have been described by Hertig, Rock, White, and Adams (Table II[15]). Marcotty's[12] much-quoted outline of the distinguishing features of older corpora is still basically accurate. Others[3, 4, 6, 13] have emphasized the importance of certain characteristics peculiar to pregnancy, among these calcium and colloid which, when present, can be considered helpful aids for identification. We[15] previously listed: (1) the greater size of the whole structure and of the cavity, (2) the more advanced development of connective tissue and vascular elements, (3) the presence of *colloid* and/or *calcium*, and (4) the presence of differently constituted lipoids as histological criteria important for delineating a corpus luteum of pregnancy. These we would substantiate and re-emphasize. The presence of colloid and/or calcium ranks as the most important feature, for all our specimens contain one or the other. In all but rare instances, *one may safely label a corpus luteum as concurrent with pregnancy if its granulosa lutein cells contain colloid material or calcium globules.*

The fourth point just mentioned was not investigated to any degree in the current study. The complicated techniques of tissue preparation make such a course as yet impractical for general use. Israel and co-workers[9] are undertaking a study of this particular question on their term or near-term specimens.

If ovarian structures other than a corpus luteum are present in the material for consideration, characteristic alterations in their development can be valuable aids in identification. The theca lutein reaction of atretic or maturing

follicles and the decidual reaction of the ovarian cortex are two changes of remarkable prominence frequently observed in later pregnancy. When either is present with a colloid-containing corpus luteum, one may be certain of a concurrent pregnancy (Table VII). Although a flourishing thecal reaction with a mole or chorion-epithelioma is well known to all, a description of a coexisting corpus luteum, if any, has been neglected.

TABLE VII. SUMMARY OF THE CHANGES IN THE OVARY DURING PREGNANCY

	FIRST TRIMESTER	SECOND TRIMESTER	THIRD TRIMESTER
Corpus luteum			
Size	Large but decreasing		Small
Cavity	Large but decreasing		Small or absent
Connective tissue	Delicate and mesenchymal		Heavy and hyalinized
Granulosa cells	Large, plump, loosely arranged		Smaller, compact
Stellate	Present	Most numerous	Present
Prickle	Usually inner one third		None seen
Vacuoles		Prominent	Few
Colloid	Present	Most	Present
Calcium		Absent	Present
Theca cells	Prominent to readily noticeable		Few or absent
Theca lutein reaction	Moderate in about one half		Flourishing
Decidual reaction		Infrequent	Usually prominent

From Table VII one can see that the histological development of a corpus luteum may be roughly correlated with the age of a gestation. Many characteristics may be used to aid in distinguishing an ovary or corpus luteum of *early* (through the second trimester) from that of a *late* (third trimester) pregnancy. By employing also the criteria set forth by others, one can be reasonably certain in a further subdivision of *very early* specimens (one to 3 months). Such a division of the phases of development is admittedly arbitrary even though it compares favorably with the two stages of a menstrual corpus given by Brewer.[2] Finer division is at this time impossible. It may not ever be feasible, for definite dating of a menstrual corpus or of the endometrium to the exact day of the cycle still remains impractical for most observers.

A last point of consideration relates to the functional capacity of the ovarian structures in pregnancy as depicted histologically. In the human, the corpus luteum, and indeed the ovaries, may be surgically removed without interrupting an intrauterine pregnancy. Consensus of most observers is that, after very early pregnancy, the corpus luteum is no longer essential for its maintenance.

Corpora lutea within one month of the last menstrual period have been portrayed as highly active and purposefully functioning units.[15] After this age, specimens show degenerative processes, usually most marked between the seventh and sixteenth weeks. Following this, the fourth month of pregnancy, the corpus appears inactive and changes but little until the end of pregnancy, at which time the all-important placenta is separated from its implantation site. In our patients, signs of degeneration were present throughout pregnancy.

It seems best to conclude, therefore, that:

1. The corpus luteum actively flourishes and functions during the first six weeks of pregnancy.
2. It markedly deteriorates during the eighth to the sixteenth week.
3. It is passively maintained from then on to the termination of pregnancy.
4. After this it degenerates rapidly to form a corpus albicans.

During the last trimester other evidences of activity simultaneously become manifest in the ovary by a theca lutein and decidual reaction. These reactions we must definitely attribute to the influence of extrinsic (placental) hormones. Put in another way, it may be said that early in pregnancy the ovary becomes an *end organ* which is stimulated by the continuing concentration of placental hormones. These are so significant and efficient that, after 3 months of pregnancy, the pituitary, both ovaries and adrenals could probably be removed without causing any apparent hormone deficit.[17] One of us (W. W. N.) does not believe that such thecal elements function as a "thecal gland," for evidence points only to their being "awakened" by the prolonged and intensive influence of hormone stimulation. When a mole or chorionepithelioma is present, the same results are observed. The other of us (R. R. G.) is uncertain whether these cells "function" even though such function may not be essential to pregnancy.

No new thecal elements are available within the corpus luteum for continued stimulation. Evidences of slow deterioration can be observed in all the elements of a corpus throughout pregnancy. Eventually they become exhausted and wear out. Following delivery and the subsequent loss of hormone support, the elements carried by such stimulation degenerate rapidly. New, quiescent, continuously available thecal elements of atretic and developing follicles are found throughout pregnancy. Time is required for these to be "activated" and/or luteinized. The same holds true for stromal elements which react to form a decidual change. There is, therefore, a gradual subsidence of luteinized thecal elements within the corpus luteum in the face of lush reactions in other structures. With the interruption of pregnancy, these latter also rapidly disappear.

We conclude that the ovary during the larger portion of pregnancy histologically appears to act only as an end organ, influenced by extrinsic substances, obviously of placental origin. It seems unlikely to one of us (W. W. N.) that histochemical studies on the ovaries from late pregnancy will show much functional activity of its structures. It is obvious that the other author has a few mental reservations about the possible low-grade function of the corpus luteum after the sixth week and also the possible function of the theca lutein reaction of later pregnancy. He considers the fact that a pregnancy continues normally with removal of the ovaries to be inadequate evidence that ovaries have no function when present.

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STUDIES ON THE ABSORPTION OF VITAMIN B_{12} IN HUMAN PREGNANCY WITH ESPECIAL REFERENCE TO THE EFFECT OF D-SORBITOL

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THE absorption of orally administered vitamin B_{12} is significantly increased by pregnancy.[1] Until recently no other physical condition and no pharmacological agent was known to increase absorption of this vitamin from the gastrointestinal tract of normal adults. Recently, however, evidence has been obtained[2-4] which clearly demonstrates that, when the vitamin is administered with D-sorbitol, absorption is significantly enhanced.

In order to gather more data on the absorption-enhancing ability of D-sorbitol and to learn more about the absorption of vitamin B_{12} during pregnancy, two studies were conducted on patients registered for prenatal care and delivery on the obstetrical service of the Johns Hopkins Hospital. The first study compared the effects of orally administered vitamin B_{12}—with and without D-sorbitol—and intramuscular injections of the vitamin on the serum B_{12} levels in patients during the last month of pregnancy and in both mother and fetus at parturition. The purpose of the second study was to determine whether vitamin B_{12} crossed the human placenta.

Materials and Methods

In the first study, 26 women were given vitamin B_{12} supplementation. At the beginning of the investigation all were 36 weeks pregnant; no other factor entered into their selection. Eight of the patients were given 50 mcg. of vitamin B_{12} by intramuscular injection each week until delivery. The other 18 individuals received vitamin B_{12} orally for the same length of time. Of these, 10 received 50 mcg. of the vitamin daily in an aqueous solution; the remaining 8 received 50 mcg. of the vitamin each day in a vitamin-mineral preparation containing D-sorbitol.* Fifteen cubic centimeters of the D-sorbitol preparation contained:

Vitamin B_{12} (cyanocobalamin)	25 mcg.
Vitamin B_6 (pyridoxine)	6 mg.
Ferric pyrophosphate (36 mg. elemental iron)	300 mg.
Folic acid	1.5 mg.
D-sorbitol	60%

*Vi-Sorbin, Smith, Kline and French Laboratories, Philadelphia, Pa.

Determinations of serum B_{12} levels were made on each patient before therapy and then weekly until delivery. At the time of parturition blood for serum B_{12} determinations was collected from the fetal umbilical vein and from a maternal antecubital vein.

In the second study, 14 pregnant individuals were each given 100 mcg. of vitamin B_{12} by intramuscular injection from 1 to 22 hours before delivery (Table IV). The majority were in active labor when they received the injection. Some were delivered per vaginam and others, by elective cesarean section. Prior to injection a "control" sample of maternal venous blood was obtained. At the time of delivery blood for serum B_{12} determination was collected from the fetal umbilical vein and from a maternal antecubital vein.

Serum B_{12} levels in both studies were determined through microbiological assays with the use of *Lactobacillus leichmannii* A.P.C.C. No. 7839 as the test organism.

Results

The serum B_{12} levels observed in women who received medication from the thirty-sixth week of pregnancy until delivery are summarized in Tables I to III. Although serum levels were determined weekly, only those determined during weeks 38-39 and at delivery are presented.

TABLE I. PATIENT RESPONSE TO 50 MCG. VITAMIN B_{12} WEEKLY BY INTRAMUSCULAR INJECTION

	SERUM VITAMIN B_{12} LEVELS ($\mu\mu$G/ML.)			
	MATERNAL CONCENTRATION			
PATIENT	BEFORE THERAPY (WEEK 36 OF PREGNANCY)	WEEKS 38-39 OF PREGNANCY	AT DELIVERY	FETAL CONCENTRATION AT DELIVERY
1	286	420	350	875
2	105	134	169	408
3	146	262	227	414
4	99	251	350	717
5	227	379	397	1,003
6	187	187	198	571
7	106	461	356	851
8	257	647	397	460
Average	176.6	342.6	305.2	662.4

TABLE II. PATIENT RESPONSE TO 50 MCG. VITAMIN B_{12} IN AQUEOUS SOLUTION DAILY BY MOUTH

	SERUM VITAMIN B_{12} LEVELS ($\mu\mu$G/ML.)			
	MATERNAL CONCENTRATION			
PATIENT	BEFORE THERAPY (WEEK 36 OF PREGNANCY)	WEEKS 38-39 OF PREGNANCY	AT DELIVERY	FETAL CONCENTRATION AT DELIVERY
9	88	134	128	255
10	198	152	140	502
11	70	175	175	190
12	105	76	81	152
13	81	88	76	542
14	70	122	145	670
15	50	70	87	402
16	82	56	64	210
17	204	100	175	250
18	99	175	175	220
Average	104.7	114.8	124.6	339.3

As indicated in Table I, after 2 to 3 weeks of therapy patients who received 50 mcg. of vitamin B_{12} each week by intramuscular injection had serum

B_{12} concentrations significantly higher than pretherapy levels ($P<.05$). At delivery serum levels showed a slight but not a significant decrease from those obtained at weeks 38-39; levels were still significantly above pretherapy values ($P<.05$). Fetal serum B_{12} contents were significantly higher than the maternal ($P<.05$).

Individuals who received 50 mcg. of vitamin B_{12} each day in an aqueous solution showed no significant increase over pretherapy serum levels by weeks 38-39 or at the time of delivery ($P>.05$). Fetal serum B_{12} concentrations were significantly higher than maternal ($P < .05$) (Table II).

TABLE III. PATIENT RESPONSE TO 50 MCG. VITAMIN B_{12} IN 60 PER CENT D-SORBITOL SOLUTION DAILY BY MOUTH

	SERUM VITAMIN B_{12} LEVELS ($\mu\mu$G/ML.)			
	MATERNAL CONCENTRATION			
PATIENT	BEFORE THERAPY (WEEK 36 OF PREGNANCY)	WEEKS 38-39 OF PREGNANCY	AT DELIVERY	FETAL CONCENTRATION AT DELIVERY
19	151	192	228	466
20	110	216	210	1,500
21	58	140	157	379
22	105	286	210	379
23	157	157	128	356
24	134	238	234	357
25	140	455	210	466
26	163	426	280	1,679
Average	127.3	263.7	207.1	697.8

As shown in Table III, patients who received 50 mcg. of vitamin B_{12} each day in solution with D-sorbitol had a response comparable to that of the patients who received the vitamin by weekly intramuscular injection. By weeks 38-39 of pregnancy these women had a significant rise in serum B_{12} levels ($P<.05$) and a slight but not significant decrease at delivery. At parturition, serum levels were significantly above pretherapy concentrations ($P<.05$). Fetal serum B_{12} levels were significantly higher than maternal levels ($P<.05$). Analyses for covariance, that is, correcting for differences in pretherapy serum B_{12} levels, were made to determine whether the differences between the three types of medication were significant. Analysis showed that by weeks 38-39 there was no significant difference between the levels of individuals who received the intramuscular injection and those who received the D-sorbitol preparation ($P>.05$). Both groups, however, had serum B_{12} levels significantly higher than the group who received the aqueous preparation ($P<.01$).

At delivery the patients who received the intramuscular injection had serum B_{12} levels higher than those who received the D-sorbitol preparation ($P<.05$), while those who had received the D-sorbitol had higher contents than those who received the aqueous preparation ($P<.05$).

A comparison of fetal serum B_{12} showed no significant difference between levels obtained following the intramuscular and D-sorbitol regimens. Both, however, produced concentrations that were significantly higher than those obtained when vitamin B_{12} was given in aqueous solution ($P<.05$).

Results of the study to determine whether vitamin B_{12} crosses the human placenta are summarized in Table IV. The data reveal that when the vitamin was injected less than 4 to 6 hours before parturition, the maternal levels were higher than the fetal. On the other hand, when the vitamin was injected more than 4 to 6 hours before parturition, fetal levels were higher than maternal.

TABLE IV. PATIENT RESPONSE TO INTRAMUSCULAR VITAMIN B_{12} GIVEN JUST PRIOR TO PARTURITION

PATIENT	HOURS BETWEEN B_{12} INJECTION AND PARTURITION	SERUM VITAMIN B_{12} LEVEL AT PARTURITION ($\mu\mu$G/ML.)		DIFFERENCE*
		MOTHER	FETUS	
1	1	1,700	575	+1,125
2	1.7	1,350	475	+ 875
3	3	1,325	800	+ 525
4	3	825	500	+ 325
5	3	1,000	800	+ 200
6	3.5	1,050	525	+ 525
7	3.5	1,050	575	+ 475
8	4	1,600	1,400	+ 200
9	4	1,075	1,375	− 300
10	6	750	1,125	− 375
11	6	775	500	− 275
12	7.5	500	700	− 200
13	12	800	1,275	− 475
14	22	650	1,100	− 450

* + Mother higher than fetus.
− Fetus higher than mother.

Comment

Shortly after it was observed that D-sorbitol increased absorption of vitamin B_{12} from the gastrointestinal tract in normal men,[2] a series of studies were performed to determine the effect of D-sorbitol on vitamin B_{12} absorption under other conditions and to ascertain the optimum combination of D-sorbitol and vitamin B_{12}. In the evaluation herein reported in pregnant women a formulary presenting 50 mcg. of the vitamin daily was used. We have since established that 25 mcg. of vitamin B_{12} daily, in a 60 per cent solution of D-sorbitol, is as effective.

Increased absorption of vitamin B_{12} from the gastrointestinal tract in pregnant women by the administration of a vitamin-mineral preparation containing vitamin B_{12} and D-sorbitol is clearly demonstrated in this series of studies. Indeed, it has been shown that the combination can produce serum B_{12} levels that, at the end of gestation, equal those obtained following intramuscular injection of the vitamin. The data also disclose that the increases in maternal serum B_{12} levels are reflected in higher fetal levels.

Whether it is of value to increase serum B_{12} levels in either the mother or the fetus is debatable. It has been noted, however, that pregnant women in general have vitamin B_{12} serum levels lower than those of normal, nonpregnant women of comparable age[3] and that during the later stages of pregnancy there is a significant fall in serum B_{12} levels. Furthermore, the low levels of vitamin B_{12} are associated with a reduced glutathione content of maternal red cells.[6] While these aberrations may not be harmful to mother or fetus, there is enough evidence to cause speculation that a certain fetal level of vitamin B_{12} may be necessary in certain as yet unspecified stages of intrauterine life, for the proper development of unspecified fetal organs, for example, the thyroid gland or bone.

Summary and Conclusions

Vitamin B_{12} serum levels were determined in pregnant women in the last month of gestation in order to compare patient response to different vitamin

B_{12} regimens. The regimens were: 50 mcg. of vitamin B_{12} in aqueous solution given orally each day, 50 mcg. of the vitamin in a vitamin-mineral preparation containing 60 per cent D-sorbitol given orally each day, and 50 mcg. of the vitamin given by intramuscular injection each week. It was found that the daily administration of aqueous B_{12} did not raise the maternal serum level. When vitamin B_{12} was administered with D-sorbitol, however, the serum concentration not only was increased significantly but almost equaled the rise produced by weekly intramuscular injections of the vitamin. Fetal serum B_{12} levels were equally high under the D-sorbitol and intramuscular regimens, and both were significantly higher than fetal levels following the aqueous therapy.

Further study showed that vitamin B_{12} crosses the human placenta and that fetal serum levels of the vitamin are directly affected by maternal levels.

It is apparent from the results of this study that the vitamin-mineral preparation containing D-sorbitol is a particularly effective method of administering vitamin B_{12}. Although it is an oral preparation, it is capable of increasing serum B_{12} levels to an extent comparable to those obtained with intramuscular injections of the vitamin.

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BLOOD STUDIES IN NORMAL PREGNANCY AND THE NEWBORN: THE EFFECTS OF IRON AND CALCIUM ADMINISTRATION*

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PREVIOUS observations have been made on the hematologic changes and the iron metabolism of pregnancy.[1-7] The variations in serum calcium levels during pregnancy in patients taking calcium and vitamin D have also been studied.[8]

There is disagreement as to whether or not there is a physiologic anemia of pregnancy.[4, 5, 6] The hemodilution of pregnancy in the presence of an increase of total hemoglobin mass[9] does not necessarily result in the development of anemia in the pregnant woman. Nevertheless, the routine prophylactic administration of iron for the prevention of anemia of the mother or fetus is widespread.

Although the healthy pregnant woman would be expected to obtain an adequate amount of calcium in her normal diet (one quart of milk supplies over 1 Gm. of calcium), there have long been influences from various sources which urge that additional calcium, in the form of medications, should be administered. These influences stem from patients themselves, a segment of the dental profession, and the advertisements of some pharmaceutical concerns.

Dieckmann and co-workers[7] found that supplementary amounts of calcium, phosphorus, iron, and vitamins A and D taken during pregnancy resulted in no significant differences in the serum calcium, phosphorus, protein, or hematocrit and hemoglobin levels when compared to the levels in pregnant controls not taking supplements. There were also no changes in the duration of labor nor the amount of postpartum blood loss, and no variations in the condition of the newborn resulting from these differences in the dietary intake. The intake requirements in the latter half of pregnancy, according to the National Research Council,[10] are 15 mg. of iron and 1.5 Gm. of calcium daily.

The serum iron in normal pregnancy varies only slightly immediately after administration of iron.[11] The serum iron levels obtained in this study can therefore be considered as not subject to significant fluctuations during the day.

Eastman[12] gives the total calcium content of the fetus at term as 25 Gm., and about two thirds of this amount is taken up by the fetus during the last month of gestation. The fetus contains a total of 375 mg. of iron at term, while

*This project was supported by a grant from Ortho Research Foundation, Raritan, N. J.

the mother has stored a daily average of 3.2 mg. of iron during the entire gestation. Eastman does not consider the mother anemic and does not give iron medication unless the hemoglobin is below 10.0 Gm. per cent, the red cell count below 3.5 million per cubic millimeter, or the hematocrit below 30 per cent. He found the incidence of anemia to be 10 per cent among his pregnant patients. This incidence varies widely, depending mainly on the nutritional status of the patient. The daily intake requirement of 15 mg. of iron is provided by an adequate diet.

Calcium traverses the placenta readily, according to the experimental work with Ca^{45} in pregnant animals, although some barrier action may be present.[13] The level of serum calcium, however, is known to be quite stable, even in the presence of postpartum osteoporosis.[14] This osteoporosis, however, may be the result of a gross abnormality of calcium metabolism rather than of insufficient calcium intake.

The present work was undertaken in an effort to evaluate the effect of iron and calcium administration on the mother during pregnancy as shown by quantitative blood studies, and the effect of iron administration to the mother on the blood of the infant at birth.

Methods

A control study was made on a group of 16 normal, nonpregnant women in the childbearing age, none of whom were receiving calcium or iron from other than dietary sources. Specimens of blood drawn from these subjects were analyzed for hemoglobin, hematocrit, serum iron, and serum calcium.

A parallel series of 69 pregnant patients, none of whom were anemic and all on adequate diets, was studied throughout pregnancy. Blood specimens were taken during the first trimester and afterward at three or four additional examinations throughout gestation and these were likewise analyzed for hemoglobin, hematocrit, serum iron, and serum calcium.

Specimens of blood were then taken immediately after delivery from 64 of these same patients and analyzed for hemoglobin, hematocrit, and serum iron. Of these 64 mothers, 24 had taken ferrous calcium citrate* (each tablet containing 25 mg. iron and 85 mg. calcium) during the pregnancy, 19 had taken various other iron preparations, and 21 received no iron. The dosage of ferrous calcium citrate consisted of 6 tablets daily. In addition to the 24 patients taking ferrous calcium citrate, 6 patients received calcium in other forms, making a total of 30 patients on calcium therapy, while the remaining patients received no calcium other than that from dietary sources.

Specimens of cord blood were taken immediately at the time of delivery in 63 of the infants of these mothers, and analyzed for hemoglobin, hematocrit, and serum iron.

Serum calcium was determined by the permanganate titration with the Clark-Collip[15] modification of the Kramer-Tisdall method. Serum iron was determined by the procedure of Kitzes and associates,[16] and hemoglobin determinations were carried out by the cyanomethemoglobin method.[17] Hematocrits were estimated after centrifugation in capillary tubes of 3 mm. inside diameter.

*Supplied by Ortho Pharmaceutical Corporation, Raritan, N. J. This compound (ferrous calcium citrate with tricalcium citrate) is marketed under the trade name Rarical.

The mean corpuscular hemoglobin concentration (MCHC) was calculated from the data in all of the specimens taken from mothers and infants according to the formula:

$$\frac{\text{Hemoglobin (grams per cent)}}{\text{Hematocrit (per cent)}} \times 100 = \text{MCHC}$$

The discrepancy in total numbers among the original 69 mothers, 64 mothers at delivery, and 63 infants at delivery, can be explained by the loss of some specimens at the time of delivery as a result of technical factors. The laboratory results were analyzed statistically according to Mainland.[18]

Results

The average values in normal, nonpregnant women (Table I) may be compared with those obtained in patients at the start of pregnancy, near term, at delivery, and in the cord blood of newborn infants (Tables II to VI).

TABLE I. AVERAGE VALUES OF 16 NORMAL NONPREGNANT WOMEN

	TOTAL RANGE	AVERAGE	S.D.*
Hemoglobin (Gm. %)	12.1 – 14.6	13.2	± 0.65
Hematocrit (%)	40 – 47	43.5	± 2.4
MCHC (%)	28.1 – 32.0	30.5	± 1.1
Serum iron (μg %)	43 – 178	114	± 39
Serum calcium (mg. %)	10.5 – 11.4	10.8	± 0.31

*S.D. $= \sqrt{\Sigma \frac{d^2}{n-1}}$, where d = average deviation, n = number of determinations.

There was no significant difference in calcium levels between the subjects who received calcium medication in various forms and the group who received no calcium medication during the pregnancy (Table II).

TABLE II. SERUM CALCIUM VALUES DURING PREGNANCY

MEDICATION	NO CALCIUM (MG. %)	FERROUS CALCIUM CITRATE (MG. %)	OTHER CALCIUM (MG. %)
Number of subjects	33	24	6
Starting Level.—			
Total range	9.7-12.0	9.5-11.4	9.5-10.8
Average	10.6	10.4	10.3
S. D.	±0.51	±0.48	±0.49
Level Near Term.—			
Total range	9.3-11.5	9.1-11.1	9.6-11.2
Average	10.5	10.2	10.5
S. D.	±0.52	±0.61	±0.53

Interpretation: No significant differences pertaining to therapy.

The serum iron and hemoglobin studies are summarized in Tables III and IV. The average for the serum iron in mothers at delivery is higher than in the nonpregnant women, and highest in the group who were taking ferrous calcium citrate, but no statistically significant differences could be calculated (Table III) among the groups taking ferrous calcium citrate, other iron preparations, or no iron. The average hemoglobin concentration of these groups is similar and no statistical differences are apparent. In the newborn infants, however, some differences are apparent in association with these three groups of mothers.

Where no iron was prescribed to the mother both the serum iron and the hemoglobin of the infant were lower than in the group that received iron supplements and these differences are statistically significant (Table IV).

TABLE III. HEMOGLOBIN AND SERUM IRON IN MOTHERS AT DELIVERY

MEDICATION	NO IRON	FERROUS CALCIUM CITRATE	OTHER IRON
Number of subjects	21	24	19
Hemoglobin (Gm. %).—			
Total range	11.1-15.3	10.6-15.2	11.4-15.3
Average	12.6	13.2	12.9
S. D.	±1.1	±1.3	±1.1
Serum Iron (μg %).—			
Total range	43-223	68-328	56-167
Average	125	152	127
S. D.	±45	±52	±28

Interpretation: No significant differences pertaining to therapy.

TABLE IV. HEMOGLOBIN AND SERUM IRON IN NEWBORN INFANTS (CORD BLOOD) OF MOTHERS ON VARIOUS MEDICATIONS DURING PREGNANCY

MEDICATION	NO IRON	FERROUS CALCIUM CITRATE	OTHER IRON
Number of subjects	21	23	19
Hemoglobin (Gm. %).—			
Total range	11.8-16.5	13.9-17.8	13.7-17.8
Average	14.8	15.9	15.9
S. D.	±1.5	±1.1	±1.2
Serum Iron (μg %).—			
Total range	96-223	135-292	116-284
Average	159	201	198
S. D.	±34	±45	±39

Interpretation: Significant differences in Ferrous Calcium Citrate and Other Iron therapy groups and group receiving no iron (see text).

TABLE V. COMPARISON OF MCHC LEVELS EARLY IN PREGNANCY, NEAR TERM, AND AT DELIVERY IN MOTHERS AFTER VARIOUS MEDICATION

MEDICATION	NO IRON	FERROUS CALCIUM CITRATE	OTHER IRON
Number of subjects	16	23	20
Early pregnancy			
Total range	29.3-32.1	27.5-34.2	28.5-32.9
Average	30.7	30.9	31.3
S. D.	±0.9	±2.0	±1.5
Near term			
Total range	29.7-33.4	26.5-35.5	27.8-33.6
Average	31.4	30.7	31.4
S. D.	±1.2	±1.9	±1.5
At delivery			
Total range	29.5-34.2	26.8-34.2	28.5-35.3
Average	30.7	30.9	31.3
S. D.	±0.9	±2.0	±1.5

Interpretation: No significant differences in early pregnancy, near term, or at delivery, regardless of therapy.

No differences were noted in the MCHC levels in mothers from the early stages of pregnancy through the last trimester and at the time of delivery, whether they received no iron, ferrous calcium citrate, or other iron preparations (Table V). But here also, the cord blood of infants from mothers of the three

groups did show some differences (Table VI). The group who received iron medication showed significantly higher cord MCHC values than the group who took no iron.

TABLE VI. COMPARISON OF MCHC LEVELS IN CORD BLOOD OF INFANTS FROM MOTHERS ON VARIOUS MEDICATIONS

MEDICATION	NO IRON	FERROUS CALCIUM CITRATE	OTHER IRON
Number of subjects	16	21	19
Total range	27.6-21.3	27.3-33.3	27.6-33.8
Average	29.2	30.4	30.1
S. D.	±1.1	±1.8	±1.7

Interpretation: Significant differences (at 5 per cent level) in Ferrous Calcium Citrate and Other Iron therapy groups and group receiving no iron.

We consider differences as statistically significant when P is less than 0.05, or at the 5 per cent level.[18]

None of the patients who took ferrous calcium citrate complained of gastrointestinal discomfort as a result of the drug. It was well tolerated and caused no constipation or diarrhea.

There were no apparent clinical differences in the patients regardless of therapy, nor were there any observable variations among the infants after birth which could be attributed to the previous medication given to the mother.

Comment

It was expected, because of the physiologic hemodilution during pregnancy, that the patients in this study would show some decrease in hemoglobin or MCHC.[1] No significant changes were noted, however.

According to Smith and associates,[2] the serum iron does not vary between nonpregnant and pregnant subjects. Our data show a slightly higher average value at delivery (Tables I and III). Also, the serum iron in the newborn infants (Table IV) ranges significantly higher than in the mothers.[2]

All forms of iron gave significantly higher serum iron and hemoglobin values in the newborn, and this may be taken to denote some advantage in the routine administration of iron during pregnancy. One cannot infer from these higher serum iron values, however, that more efficient storage of iron occurs in the infants nor that there follows a lower incidence of anemia later in infancy. Smith and his co-workers[3] state that the stores of transplacentally acquired fetal iron cannot be predicted from the fetal hemoglobin values at birth. The infant depends on its original iron stores during the first months of life. Low fetal storage can be suspected when maternal hemoglobin is very low in late pregnancy.[19] None of the patients in our study were in this group.

The transfer of iron across the placenta favors the fetus, as indicated by the consistently higher level of iron in the infant's serum when compared to the mother's level. The exact mechanism of transfer is not known, but ferritin plays a role.[20, 21] In animal experiments the amount of iron supplied to the fetus from the maternal plasma appears to be sufficient to account for the iron retained by the fetus during growth.[22] The gastrointestinal absorption of iron during pregnancy increases as gestation progresses, but larger oral doses have

no advantages over smaller ones.[23] Coons[24] showed that eggs and meat were the most important items of diet necessary for adequate iron absorption during pregnancy. The positive daily iron balance in the mothers in that study varied from 0.88 to 6.97 mg. daily. The fetus received about 0.4 mg. of iron daily during the first two trimesters, and about 4.7 mg. of iron daily during the last trimester.[24]

Our observations are in agreement with the previous findings of Newman[8] that the administration of calcium during pregnancy has no effect on the serum calcium level. Although Newman differentiated the serum calcium into ionized and unionized fractions from studies of serum protein levels, our experiments did not include such analyses. In view of the clinical status of our patients, however, we have assumed that they had normal serum protein levels for pregnancy. It therefore appears that with an adequate diet, the additional intake of calcium is of doubtful value.

In view of our findings there does not appear to be sufficient justification for the routine administration of iron during pregnancy. However, a similar study extended into the first year of the infant's life, with hemoglobin and iron studies continued to 1 year of age, might give a more definitive answer.[25]

Summary

The mother's serum calcium levels appear to remain unchanged, whether or not calcium is administered during pregnancy.

The administration of medicinal iron during normal pregnancy gives a significantly higher level of hemoglobin and serum iron in the infant's cord blood, and no differences in the mother, when campared to levels in subjects who receive no iron. The routine administration of iron cannot be justified from the findings in this study based on hemoglobin and serum iron data.

No significant variations in MCHC (mean corpuscular hemoglobin concentration) were found to occur during pregnancy or at delivery in the mothers, whether or not iron was administered during pregnancy. In the cord blood of the newborn, however, iron therapy caused significantly higher MCHC levels when compared to the levels of those who received no iron.

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THE EFFECT OF INTRANASAL ADMINISTRATION OF OXYTOCIN ON THE LET-DOWN OF MILK IN LACTATING WOMEN

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THE smooth course of breast feeding is related to adequate function of the let-down reflex. Stimulation of the nipple in the lactating woman results in the release of an oxytocic factor into the blood stream through the mediation of the central nervous system and the posterior lobe of the pituitary gland. This substance then acts on the myoepithelial elements surrounding the alveoli of the breast, causing them to contract and force milk into the larger ducts where it is more readily available to the baby. The let-down reflex is sensitive to psychological stimuli. It can be conditioned so that the mother learns to let down her milk to the sound of the baby crying or other associated stimuli.[1] Furthermore, it can be inhibited by pain or emotional distractions, so that less milk is available to the baby.[2, 3]

Failure in breast feeding is related to failure of the let-down reflex. It has been shown[4] that women who needed to give their babies supplemental formulas actually retained 47 per cent of their milk in the breasts. Neither the sucking baby nor the breast pump could remove it. Most of it could be removed, however, by setting off the let-down reflex artificially with injections of oxytocin. In a study of 103 nursing mothers it was found that mothers whose babies did not need supplemental bottles had significantly more symptoms and signs of let-down than mothers whose babies required supplemental feedings. The reflex appeared to work less erratically in the successful mothers. In these there was significantly less variation in the amount of milk the baby obtained from one feeding to the next. Failure of the let-down reflex may also predispose to the development of nipple lesions, mastitis, and breast abscess.[5, 6]

In relaxed, confident women with babies who suck eagerly the let-down reflex usually functions well. A high proportion of new mothers in our culture are tense at the start of breast feeding, however. Furthermore, their babies are often taught to suck the bottle in the nursery and are brought to the mother on a rigid schedule when they are not necessarily hungry. Under these circumstances the vigorous sucking that sets off the let-down reflex may be absent.

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It is often impossible to change hospital routines and the psychological factors responsible for the failure of the let-down reflex. Artificial production of the reflex may therefore be of value. Subcutaneous, intramuscular, and intravenous injections of Pitocin are effective[7, 8, 9] but repeated injections are disagreeable for the mother and require the presence of medical personnel. Since oxytocin has been used intranasally for the induction of labor,[10] it was suggested by Quinlan[11] that the intranasal route might be preferable in the management of lactation. The purpose of this study was to test the practicability and effectiveness of intranasal oxytocin in setting off the let-down reflex.

Methods

Nineteen women from the postpartum floor of the University of Mississippi Hospital were used as subjects. Their average age was 22.7 years with a range from 15 to 35 years. Seven were primiparas and twelve multiparas. Eight of the multiparas had breast fed the last child for 2 months or more (up to 12 months) while 4 had not done so, or had made abortive attempts at breast feeding. All the women expressed a desire to breast feed their babies at least for a while after they left the hospital. At the time of the study the breast feeding routine was such that the women were first given their babies to nurse at varying times up to 24 hours after delivery. Babies were then brought to their mothers every 4 hours and left with them for from 30 to 45 minutes. No restrictions were placed on the amount of suckling given during this time. All the mothers used in the study had had milk in their breasts for at least 6 hours and the majority for over 12 hours. Experiments were performed at a mean of 79 hours after delivery with a range of from 34 to 167 hours.

A total of twenty studies was performed, one subject being used twice. Each study consisted of three experiments, performed 2 hours after each of three successive nursing periods. In 15 instances the three experiments were performed at 7:00 A.M., 11:00 A.M., and 3:00 P.M., and in 5 they were performed at 11:00 A.M., 3:00 P.M., and 7:00 P.M. The subjects were told that a test was being made of their milk. Cooperation and rapport were good at all times.

Each experiment was conducted in the same manner. The subject lay on her back or side in a comfortable position. One breast was pumped with an electric breast pump for 5 minutes. Intermittent suction was applied at a rate of 25 to 30 times a minute by finger control in such a way that the suction pressure rose to 5 to 6 inches of mercury and was then released. There was then a 5 minute delay period, after which the same breast was pumped again in a similar manner for another 5 minutes. The same breast was used in all three experiments on the same woman. The only difference was in the procedure used during the delay period. In one experiment nothing was done (experiment A). In the second, a cotton applicator soaked in 0.5 c.c. saline was inserted into one nostril: at the end of the 5 minute delay period this was removed and a similarly soaked applicator inserted into the same nostril for the duration of the second period of pumping (experiment B). In the third experiment, 0.5 c.c. oxytocin* was used instead of saline and in the same manner (experiment C). The order of the experiments was varied so that in 7 women experiment A was performed first, in 7 experiment B, and in 6 experiment C.

*Pitocin, Parke, Davis & Company.

The amount of milk obtained in each 5 minute period of pumping was measured in cubic centimeters. In addition, as an indication of the occurrence of let-down of milk, the subjects were asked during each period of pumping whether they noted pain anywhere, and, if so, where. A response of abdominal pain was taken to indicate uterine contraction. The presence or absence of milk dripping from the breast opposite to that being pumped was also recorded.

Results

The mean amounts of milk obtained in the two 5 minute periods of pumping are shown in Table I. Mean amounts obtained in the first 5 minutes were similar. In the second 5 minute period less milk was obtained than in the first period in the control experiments (A and B), whereas considerably more was obtained in the oxytocin experiments (C).

TABLE I. MILK OBTAINED BEFORE AND AFTER INTRANASAL APPLICATION OF SALINE AND OXYTOCIN

TYPE OF EXPERIMENT	NUMBER OF EXPERIMENTS	MILK (MEAN NO. OF C.C.)		MEAN DIFFERENCE
		BEFORE	AFTER	
A, no application	20	13.10	7.20	− 5.90
B, intranasal saline	20	15.25	6.15	− 9.10
C, intranasal oxytocin	20	13.25	27.85	+14.60*

*Highly significant difference when compared with control and with saline groups. P = less than .01.

Comparison between groups in the differences in amounts of milk obtained in the first and second periods of pumping showed a highly significant difference between experiments C and A and between experiments C and B. The difference between experiments A and B was not significant.

These findings are exemplified by the fact that in experiment A the amount of milk obtained in the second period was less than that obtained in the first period in 18 patients and more in only 2. In experiment B the amount obtained in the second period was less in 17, the same in 2, and more in one. In the oxytocin experiments the amount obtained in the second period was more than that obtained in the first in 17, the same in 2, and less in only one.

The symptoms and signs of let-down are shown in Table II. None occurred during the first pumping period. During the second pumping period they were noted nine times in the oxytocin experiments, but only twice in control experiment B, and not at all in control experiment A.

TABLE II. SYMPTOMS AND SIGNS OF LET-DOWN AFTER INTRANASAL APPLICATIONS OF SALINE AND OXYTOCIN

TYPE OF EXPERIMENT	NUMBER OF EXPERIMENTS	UTERINE CRAMPS	MILK OPPOSITE BREAST	TOTAL SYMPTOMS AND SIGNS
A, no application	20	0	0	0
B, intranasal saline	20	2	0	2
C, intranasal Pitocin	20	6	3	9

Undesirable side effects of oxytocin were minimal. Mild disapproval of the intranasal applicator was noted on occasion. Watering of the eyes occurred commonly with the application of oxytocin but stopped within 2 minutes. In no case was it necessary to discontinue the experiment because of unfavorable reactions.

Comment

The demonstration of increases in milk flow after the application of oxytocin indicates that this substance is absorbed from the nasal mucosa. Presumably it enters the blood stream and then acts on the myoepithelial elements surrounding the alveoli of the breast in the same manner as when it is administered parenterally.

It was considered possible that the breast pump itself might stimulate the reflex and confuse the findings. However, women who are not accustomed to using a breast pump usually take some time to learn to let down their milk to it, and, indeed, they may never respond as fully as to the baby. The increased flow of milk found in the oxytocin experiments cannot be accounted for by natural let-down stimulated by the breast pump since the breast pump did not have this effect in control experiments A and B.

The 5 minute period allowed for absorption was chosen empirically and the intranasal source of oxytocin was maintained by continuing the application during the second period of pumping. It is possible that oxytocin may be absorbed more quickly than this and that less time is needed for such absorption. Certainly no longer time is necessary.

The intranasal dose of oxytocin given was 0.5 c.c. (5 units) in each of the two applications. Again, this was an empirical choice. One dose of 0.5 c.c. might have been sufficient and, indeed, even less may be necessary.

Cotton applicators soaked in oxytocin solution were used as the method of administration because of the desirability of maintaining the oxytocin in contact with the nasal mucosa. An alternative method might be the insertion of drops of oxytocin solution into the nose by means of a dropper. Preliminary studies had suggested that drops might be more uncomfortable and that the solution ran down into the pharynx rather than remaining in the nose. Quinlan,[11] however, reports success with the use of oxytocin nose drops in the clinical management of patients.

Our results suggest that the intranasal application of 0.5 to 1.0 c.c. of oxytocin, given about 5 minutes before the baby starts to nurse, may help the mother overcome inhibition of the let-down reflex. Thus she may be helped to breast feed successfully.

The use of intranasal oxytocin is, however, essentially symptomatic treatment. Attention to the causes of inhibition and failure of the let-down reflex will reduce the need for medication. Particularly important are sucking stimulation and emotional factors.

Since vigorous sucking is the primary stimulus which sets off the let-down reflex, the strength of the baby's sucking is a matter of concern. When rooming-in of mother and baby is not possible, it is of advantage to bring the baby in to the mother whenever he is hungry, thus allowing him to nurse when his sucking is likely to be most vigorous. Sucking a bottle rapidly interferes with the strength of the sucking reflex.[12] Thus, when supplementation is necessary, it can be given after breast feeding and by spoon or cup rather than by bottle.

Attention to emotional factors starts in the antepartal period. Unfamiliar surroundings may inhibit the let-down reflex. New mothers may be prepared for the initiation of breast feeding by allowing them to tour the hospital during pregnancy and giving them a chance to meet the nursing personnel. Specific instruction in the physiology of breast feeding and practice in holding a dummy baby in relaxed breast feeding positions[13] should be a basic part of antepartal education.

Postpartal emotional support is essential. Sympathetic help from the nursing staff is of first importance. Discomfort from sore nipples, afterpains, perineal repairs, or breast engorgement should be relieved by suitable analgesics given before nursing. Since embarrassment may inhibit the let-down reflex, freedom from interruptions and examinations by medical personnel during feeding times is of value. Finally, discussion of minor problems with a mother who has successfully breast fed her own children can help to relieve anxiety and promote relaxation.

Summary and Conclusions

1. The artificial production of the let-down (ejection) reflex by the intranasal application of oxytocin during early lactation has been tested.

2. Intranasal oxytocin produced a significant increase in the flow of milk, indicating that let-down had occurred.

3. The use of intranasal oxytocin appears to be an effective and practical method of overcoming inhibition of the let-down reflex.

4. Other methods of promoting smooth functioning of the let-down reflex are discussed.

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AN EVALUATION OF A COMBINATION OF TESTOSTERONE ENANTHATE WITH ESTRADIOL VALERATE (DELADUMONE) FOR THE INHIBITION OF LACTATION

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NUMEROUS data have been accumulated from animal experiments pertaining to the problems of lactogenesis and galactopoiesis. At present, however, no theory dealing with the initiation of lactation seems to explain adequately all the known findings. The interrelationships of prolactin and sex steroids have been studied and indications are that estrogen in small amounts induces the production of prolactin, while large doses of estrogen or testosterone inhibit its formation. It is believed that during pregnancy estrogen reduces the sensitivity of breast tissue to prolactin and simultaneously inhibits or reduces prolactin production.[1, 2] The direct action of estrogen on breast tissue is presently considered as the more important of the two actions.[3] Accordingly, it is assumed that the immediate postpartum reduction of estrogens removes the inhibitory effect upon breast tissue and induces the formation or release of prolactin. More recently Meites and Sgouris[4, 5] have demonstrated in animal experiments and in studies of breast tissues in vitro that the injection of estrogen and progesterone in the correct ratio will prevent the action of prolactin and inhibit the initiation of lactation. The ratio of the two sex hormones seems to be species specific. They found, furthermore, that by considerably increasing the amount of injected prolactin the established barrier can be broken through and lactation will ensue. These experiments would therefore imply that the important factor in inhibition of lactation is the combined action of estrogen and progesterone upon breasts which exhibit lobular-alveolar development. So far, no clinical evidence has been found to prove this in the human female, especially with regard to therapeutic inhibition of lactation. It is of interest to note that apparently the same gonadal hormones which are responsible for the lobular-alveolar development of mammary tissue during the first half of pregnancy are also instrumental in suppression of lactogenesis.

Since Parkes and Bellerby[6] have shown that estrogen depresses lactation in mice, different short-acting estrogens and androgens, and two long-acting androgens[7, 8] have been used clinically for the inhibition of lactation. It is customary to treat patients with a standard dosage disregarding individual variations in response to the hormones, as no criteria are available to indicate

the patient's sensitivity. This is no doubt responsible for some of the difficulties in achieving complete inhibition of pain, breast engorgement, and lactation in all treated patients.

Procedure

With the advent of long-acting estrogen and testosterone preparations it was considered worth while to study their effect on inhibition of lactation. A combination of testosterone enanthate and estradiol valerate dissolved in sesame oil (Deladumone*) was used in the form of a single intramuscular injection given immediately after expulsion of the placenta simultaneously with other routine injections. The majority of the patients were still under the influence of anesthesia and they were not aware of having received any treatment for suppression of lactation. Each milliliter of Deladumone contains 4 mg. of estradiol valerate and 90 mg. of testosterone enanthate. It is believed that the gradual absorption of Deladumone starts shortly after administration of the medication and that action is sustained for from 10 to 14 days. The action of Deladumone is based mainly on clinical evaluation of postmenopausal conditions because no blood level studies are available at present.

A total of 253 puerperal patients were treated with this medication. During the initial phase of the study 167 patients were divided into five small groups to determine any ill effects from this substance and to ascertain the effectiveness of different dosages on suppression of lactation. The different dosages of Deladumone were 1 c.c., 2 c.c., 2.5 c.c., 3 c.c., and 3.5 c.c. Improved results were obtained in the fifth group consisting of 50 cases in which 3.5 c.c. of Deladumone was used, which corresponds to 14 mg. of estradiol valerate and 315 mg. of testosterone enanthate (Table I). The study was, therefore, extended with the same dosage to an additional 86 patients. This group comprises, therefore, 136 cases in which a more detailed study was conducted. The patients were kept in the hospital 8 or 9 days. Observations were made and recorded daily by the same investigator concerning the condition of the breasts, lochia, and degree of uterine involution. The study was performed during the hot summer months and no restrictions were imposed on fluid consumption. Brassieres, breast binders, or analgesics were used only for the patients who developed pain with breast engorgement and/or leakage.

TABLE I. FIVE GROUPS OF PATIENTS TREATED WITH DIFFERENT DOSAGES OF DELADUMONE (PILOT STUDY)

GROUP	DOSAGE OF DELADUMONE	NUMBER OF PATIENTS TREATED	PATIENTS WITH COMPLETE FREEDOM FROM BREAST ENGORGEMENT, PAIN, OR LACTATION (LEAKAGE)	
			NO.	%
I	1 c.c.	11	None	0
II	2 c.c.	39	12	31
III	2.5 c.c.	29	14	48
IV	3 c.c.	38	18	47.3
V	3.5 c.c.	50	34	68

A maternity head nurse familiar with the patients was employed to obviate any difficulties of a thorough follow-up study. The patients were visited and examined by this nurse at regular intervals during a 6 months' period. In addition a number of them were seen in the postnatal clinic. Patients who were completely free of breast engorgement, pain, and leakage during their

*The Deladumone was supplied through the courtesy of Dr. E. C. Reifenstein, Jr., of E. R. Squibb & Sons, N. Y.

hospital stay and the follow-up period at home were designated as having "good results." Patients who developed breast engorgement, pain, or lactation for not exceeding 48 hours' duration were considered to have "partial success." All other cases were classified as "failures." In addition, the group of 136 cases was subdivided into consecutive smaller groups and the findings were analyzed. This was done to test the validity of results obtained in the pilot study and of findings resulting from investigation of relatively small groups of cases.

Results

In the 253 cases there was complete absence of any local or systemic allergic reaction. With an increasing dosage of Deladumone there was a gradually increasing percentage of "good results" and this was especially marked in Group V (Table I).

The analysis of 136 patients who received 3.5 c.c. of Deladumone showed a complete absence of breast engorgement, lactation, pain or discomfort in 77.2 per cent (Table II). No breast engorgement was experienced by 84.6 per cent, and evidence of lactation was completely absent in 81.6 per cent.

TABLE II. MANIFESTATIONS IN 136 CONSECUTIVE CASES TREATED WITH 3.5 C.C. OF DELADUMONE WHEN SUBDIVIDED INTO SMALLER GROUPS

TYPE OF MANIFESTATIONS	FIRST 50 CASES		SECOND 50 CASES		REMAINING 36 CASES		FIRST 70 CASES		REMAINING 66 CASES		TOTAL 136 CASES	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Free from breast engorgement, lactation, and pain	34	68	43	86	28	77.8	49	70	56	85.8	105	77.2
With lactation	15	30	5	10	5	13.7	19	27.1	6	9	25	18.4
With engorgement	9	18	7	14	5	13.7	14	20.6	7	10.5	21	15.4
With pain or slight discomfort	8	16	7	14	3	8.2	13	18.7	5	7.5	18	13.3

Pain or even slight discomfort was absent in 86.7 per cent and 91.1 per cent were without pain. There was a delay in the onset of breast manifestations in some patients, in 3 of these until the thirteenth postpartum day (Table III).

TABLE III. ONSET OF BREAST MANIFESTATIONS IN 31 PATIENTS IN DAYS AFTER DELIVERY

DAYS AFTER DELIVERY	NO.
4th or 5th	9
6th	8
7th or 8th	10
10th to 13th	4
No. with manifestations	31
% with manifestations	22.8

The distribution of the unfavorable features in 22.8 per cent of cases is presented in Table IV. Breast engorgement accompanied by lactation and pain was found in 6.7 per cent and by lactation and slight discomfort in 1.5 per cent of the cases. Pain or discomfort occurred only in the presence of engorgement and/or lactation. In the absence of any other manifestations breast engorgement was found in 2.9 per cent and lactation in 3.7 per cent. Breast engorgement was present with lactation in 2.9 per cent and with pain in 1.5

per cent, whereas lactation with pain or slight discomfort occurred in 3.6 per cent of the patients. Of the 31 patients with manifestations, in 51.5 per cent engorgement and lactation occurred independently.

TABLE IV. TYPE OF CLINICAL MANIFESTATIONS IN 31 PATIENTS WITH SYMPTOMS

TYPE OF MANIFESTATIONS	NO. OF CASES	% OF CASES
With engorgement	4	2.9
With lactation	5	3.7
With pain	None	None
With engorgement and lactation	4	2.9
With engorgement, lactation, and pain	9	6.7
With engorgement, lactation, and slight discomfort	2	1.5
With engorgement and pain	2	1.5
With engorgement and slight discomfort	None	None
With lactation and pain	1	0.7
With lactation and slight discomfort	4	2.9
Total cases with manifestations	31	22.8

When the duration and the degree of the manifestations were analyzed (Table V), it was found that 94.8 per cent did not have breast engorgement that lasted for more than 48 hours, 90.5 per cent were free from lactation within 48 hours, 95.6 per cent were free from pain after 24 hours, and 96.9 per cent after 48 hours. Breast engorgement was severe in only 8.1 per cent of the cases. Marked breast engorgement exceeded in duration engorgement of moderate and slight degree, whereas the duration of lactation appeared to be independent from the degree of leakage. For instance, in 3 cases slight lactation present at the onset persisted for 2 weeks. Lactation was severe to moderate in 10.3 per cent and slight in 8.1 per cent. The use of analgesics was necessary in only 3.7 per cent of the patients. No difference in response was noted between primiparous and multiparous patients and it is of importance that the recurrence of breast manifestations was completely absent in this study.

TABLE V. ANALYSIS OF THE DURATION AND THE DEGREE OF BREAST ENGORGEMENT, LACTATION, AND PAIN

	DURATION								
TYPE OF MANIFESTATION	1 DAY	2 DAYS	3 DAYS	4 DAYS	5 DAYS	7 DAYS	2 WEEKS	TOTAL NO. OF CASES	% OF 136 CASES
Engorgement.—									
Severe to considerable	None	4	2	2	2	1	None	11	8.1
Moderate	2	4	None	None	None	None	None	6	4.4
Slight to minimal	2	2	None	None	None	None	None	4	2.9
Lactation.—									
Severe to moderate	1	5	None	5	2	1	None	14	10.3
Slight to minimal	2	4	2	None	None	None	3	11	8.1
Pain.—									
Pain	6	2	1	1	2	None	None	12	8.9 (3.7 requiring analgesics)
Slight discomfort	None	2	2	1	1	None	None	6	4.4

To evaluate adverse effects of treatment, special attention was paid to the features of lochia, uterine involution, and bleeding, as well as to the menstrual pattern and signs of virilization (Table VI). The character of the lochia and

the degree of uterine involution were within normal limits, with the exception of 3 cases in which bleeding was also present. Retained secundines were found in one of them while the remaining 2 cases responded well to a short course of ergot medication. In no other instances were any blood clots passed and no treatment was required.

TABLE VI. FINDINGS INDICATING NO ADVERSE EFFECT FROM 315 MG. OF TESTOSTERONE ENANTHATE AND QUESTIONABLE ADVERSE EFFECTS FROM 14 MG. OF ESTRADIOL VALERATE

FEATURE ANALYZED	NO. OF CASES	% OF 136 CASES
Virilization	None	None
Bright red postpartum staining lasting 4 weeks	6	4.4
Uterine bleeding	3	2.2
Subinvolution of the uterus	2	1.5
Time of onset of first menses after delivery		
4 to 5 weeks post partum	12	8.9
6 to 8 weeks post partum	97	71.3
9 to 13 weeks post partum	27	19.8
Increased menstrual flow	23	16.9
Increased and prolonged menstrual flow	10	7.4
Pregnant again within 5 months after delivery	10	7.4

Postpartum bright red vaginal spotting persisted intermittently for 4 weeks in 4.4 per cent. All patients had their first menstruation within 13 weeks after delivery and 80.3 per cent within 4 to 8 weeks post partum. The periodicity of menses was found to be of a normal cyclic pattern. Changes in the first postpartum menstrual blood flow were present in 24.3 per cent of the cases when compared with the character of menstruation present prior to conception.

In 16.9 per cent the blood loss was heavier than usual, and in 7.4 per cent menstruation was also prolonged. Pregnancy occurred again 4 to 5 months after delivery in 7.4 per cent. Signs of virilization were absent in all cases.

Examination of the findings according to the classification previously outlined showed that "good results" were obtained in 84.5 per cent with regard to breast engorgement, in 81.6 per cent concerning lactation, and in 91.1 per cent in reference to pain. "Partially successful" results were obtained in 10.3 per cent in breast engorgement, in 8.8 per cent in lactation, and in 5.9 per cent in reference to pain. "Failures" were found in 5.2 per cent in breast engorgement, in 9.6 per cent in lactation, and in 3 per cent in pain.

The subdivision of 136 patients into smaller groups of consecutive cases revealed a certain discrepancy of results in the respective groups (Table II). Thus, in the first group of 50 cases, breast engorgement, lactation, and pain were completely absent in 68 per cent. In the second group of 50 cases, they were absent in 86.6 per cent, and in 77.8 per cent of the remaining 36 cases. When the 136 cases were divided into two consecutive groups, however, breast engorgement, lactation, and pain were absent in 70 per cent of the first group and in 85.8 per cent of the second group.

Lactation was present in 30 per cent of the first group and in 10 per cent of the other group consisting of 50 cases each. It was found in 27.1 per cent in the group of 70 cases but was present in only 9 per cent in the remaining 66 cases.

Comment

According to the generally accepted view, signs of breast engorgement occur on the third to the fifth postpartum day. Delayed onset of breast engorgement with or without lactation is a common finding in symptomatic cases when estrogens are used[11, 12, 16] and the present study indicates similar results.

It was noted among the patients with undesirable manifestations that inhibition of breast engorgement does not imply suppression of lactation and vice versa (Table IV). This is in conformity with the experience of others.[9, 10, 11] The action of Deladumone, however, differed with regard to recurrence of breast manifestations which frequently follow other medications.[13, 14, 15, 18, 19, 22, 25, 26] Recurrence of breast engorgement, lactation, and pain was completely absent in this study and it appears, therefore, that in this respect Deladumone is superior to other methods used. This could possibly be explained on the basis of continuous maintenance of a blood level by the long-acting steroids contained in Deladumone.

In the absence of any extensive statistical study as to what constitutes physiological postpartum menstrual loss it was difficult to evaluate changes in menstrual blood flow that might be attributable to the estrogenic component of Deladumone. They seemed to be absent in the majority of patients and when present were of little clinical importance (Table VI), as in none of them was any treatment required. Estrogenic side effects in the form of withdrawal bleeding were absent.

There were no complications attributable to testosterone enanthate. The normal onset of menstrual cycles and the occurrence of 10 conceptions within a period of 4 to 5 months following delivery suggest the absence of any adverse effects upon ovarian activity.

A brief review of some of the results obtained with different medications is presented in table form (Table VII). Different methods have been used for the postpartum "follow-up" by other investigators and for this reason it is difficult to compare exactly the results of Deladumone treatment with those of other medications.

It appears, nonetheless, on the basis of this review, that Deladumone in the dosage of 3.5 c.c. compares very favorably with other preparations in use for the inhibition of lactation and has the additional advantage of requiring only a single intramuscular injection. It cannot be stated, however, that the results presented reflect final findings with regard to the efficacy of Deladumone when used for the inhibition of lactation. The danger of drawing conclusions from relatively small groups of cases seems to be demonstrated in Table II. The discrepancy of results in cases exhibiting lactation in the two groups of 70 and 66 consecutive patients is of definite statistical significance and the findings with regard to "absence of breast engorgement, lactation, and pain" are of borderline significance. It is believed that an evaluation of a greater number of cases is required to arrive at more definite conclusions.

Summary

Two hundred and fifty-three puerperal patients were divided into five groups and treated for inhibition of lactation with an increasing dosage of Deladumone. A single intramuscular injection was given immediately following the termination of the third stage of labor.

In a group of 136 patients in whom 3.5 c.c. of Deladumone was used, 77.2 per cent were completely free from breast engorgement, pain, and lactation; 86.8 per cent were free from pain or discomfort, and 91.2 per cent were free from pain; 95.6 per cent were free from pain exceeding 24 hours' duration. In only 3.7 per cent were analgesics indicated. Comparative results were obtained with regard to breast engorgement and lactation. Recurrence of breast signs was completely absent and no untoward effects were noted from

TABLE VII. RESULTS OBTAINED BY OTHER INVESTIGATORS

NAME OF INVESTIGATOR	NO. OF CASES	MEDICATION	DOSAGE	ABSENCE OF LACTATION (%)	ABSENCE OF BREAST ENGORGEMENT (%)	ABSENCE OF PAIN (%)	REMARKS
Walsh and Stromme[12]	50	Diethylstilbestrol	10 mg., 5 mg., 5 mg. at 24 hr. intervals	26	40	46	
Dunlap and Didle[11]	95	Diethylstilbestrol	5-10 mg. daily for 7 days				Lactation not prevented in 11.6%. No diminution of mastalgia and breast engorgement
Lubin[17]	50	Diethylstilbestrol	10 mg. t.i.d. for 2 days, then 5 mg. t.i.d. for the rest of hospital stay	10	50	88	Engorgement and pain developed in 50% of patients 2 weeks after hospital discharge
Hesseltine et al.[16]	83 divided into 7 groups	Diethylstilbestrol	5 mg.-25 mg. daily for 4 to 10 days				Minimal engorgement in 33.7%. Moderate engorgement in 59% Maximal engorgement in 7.2%
Napp et al.[10]	213	Diethylstilbestrol	45 mg. after delivery, then 5 mg. t.i.d. for 3 days				Slight or no filling or engorgement in 41%
Schneeberg et al.[20]	42	Diethylstilbestrol	3 mg. daily	83	81	81	
Primrose and Tremblay[19]	48	Diethylstilbestrol	5 mg. t.i.d. for 3 days, 5 mg. b.i.d. for 3 days, 5 mg. daily for 3 days				Complete absence of lactation, engorgement, and pain in 88.8%
Morton and Miller[15]	234 divided into 4 groups. In the group of 60 cases:	Diethylstilbestrol	5-10 mg. initial dose, treated with gradually diminishing dosage for one month	93.4	93.4	93.4	Different dosage used in the four groups
Birnberg et al.[21]	145	Ethinyl estradiol	0.1 mg. t.i.d. for 3 days, then 0.05 mg. t.i.d. for 3 days, followed by 0.05 mg. daily for 3 days	58	58		Slight engorgement or slight leakage for 24-48 hours in 16%

Gershenfeld and Perlmutter[22]	238	Ethinyl estradiol	1.5 mg. t.i.d. for 6 to 9 days	40	54	57	During hospital stay engorgement absent in 74% and pain in 66%
Dunlap and Diddle[11]	125	Dienestrol	0.5-6 mg. daily for 9 days				Lactation not prevented. No diminution of mastalgia and breast engorgement in 11.2%
Kosar et al.[23]	85 divided into 4 groups	Dienestrol	1-10 mg. daily, followed by a decreasing dosage for various durations	13			
Bloom[13]	269	Dimethyl-ether stilbestrol	15 mg. I.M. and repeated in 48 hours		88		
Coulton[24]	183 divided into 7 groups. In the group of 87 cases:	Meprane (synthetic estrogen)	2-4 mg. daily for 3 to 5 days	94.3			Different dosage used in the 7 groups
Reich et al.[25]	25	Sulestrex (piperazine estrone sulfate)	18-24 mg. for 3 days, followed by 12 mg. for 2 days	92	92		
Stone et al.[26]	71	Menagen (micronized mixed estrogen)	50,000 units b.i.d. for 5 days		96	96	
Napp et al.[10]	207	Vallestril (methallenestril)	100 mg. I.M. on day of delivery, repeated if necessary				Slight or no filling or engorgement in 62%
Schneeberg et al.[20]	198 divided into 5 groups. In the group of 71 cases:	Vallestril (methallenestril)	20 mg. daily for 5 to 8 days	77	70	70	Different dosage used in the 5 groups
Nulson et al.[18]	100	Tace (chlorotrianisene)	48 mg. daily for 7 days	97			
Primrose and Tremblay[19]	68	Tace (chlorotrianisene)	12 mg. q.i.d. for 8 days				Lactation, pain, and engorgement suppressed in 62.8%

TABLE VII—CONT'D

NAME OF INVESTIGATOR	NO. OF CASES	MEDICATION	DOSAGE	ABSENCE OF LACTATION (%)	ABSENCE OF BREAST ENGORGEMENT (%)	ABSENCE OF PAIN (%)	REMARKS
Lass[27]	25	Methyltestosterone	100-350 mg. given over a period of 36 hours	80	40	40	
Garry[28]	50	Methyltestosterone	10 mg. t.i.d. for 5 days	84	44		
Rienzo[29]	92	Estan (1 tablet 5 mg. methyltestosterone and 0.25 mg. dienestrol)	2 tablets t.i.d. for 5 days	100	81.6	81.6	
Garry[28]	100	Estan (1 tablet 5 mg. methyltestosterone and 0.25 mg. dienestrol)	2 tablets t.i.d. for 5 days	97	81	83	
Primrose and Tremblay[19]	54	Premarin with methyltestosterone	3.75 mg. Premarin and 30 mg. methyltestosterone every 4 hours for 5 doses				Absence of lactation, pain and engorgement in 48.1%

the use of 315 mg. of testosterone enanthate. Side effects from 14 mg. of estradiol valerate were of no clinical significance. Attention has been drawn to the possibility of inaccuracies when only a small number of cases are investigated.

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X-RAY PELVIMETRY AND THE OUTCOME OF LABOR

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THE chief use of x-ray pelvimetry is to assist in the proper management of a patient in labor. The present study was undertaken in order to determine exactly how useful this procedure can be, when all possible information is extracted from the films.

Opinions differ as to how "accurate" x-ray pelvimetry is, and the reasons for this are complex. First of all there are three distinct aspects to the passage of the baby through the birth canal: (1) the relation of the size and shape of the bony pelvis to the size and position of the baby itself; (2) the efficiency of uterine activity; and (3) the moldability of the baby's head. X-ray pelvimetry allows us to study only the first of these: the relation of the bony pelvis to the baby at a given time. The x-rays tell nothing about the efficiency of the labor and there is no way to predict how well the fetal head will mold.

The second question which gives rise to differences of opinion as to the value of x-ray pelvimetry has to do with the technique itself and the accuracy with which it is used. When a mechanical problem is to be studied, it is necessary to obtain the highest accuracy possible in making measurements and this certainly holds for x-ray pelvimetry. Nevertheless, many techniques have been used which are demonstrably inaccurate or are incomplete, and therefore prognoses have been given which, being based on an inaccurate estimate of the mechanical situation, cannot avoid being inaccurate in regard to the clinical outcome of labor. If x-ray pelvimetry is to have any clinical accuracy it must be mechanically as accurate as it can be made.

From these films it is then necessary to determine the amount of space available in the pelvis, and to compare this with the size and position of the fetus. Measurement of the pelvis alone is not sufficient, for the question is not whether an "average" sized baby will pass through, but whether that particular baby will pass through. Failure to measure the baby is the greatest source of error in interpreting pelvimetry films.

Technical Considerations

There is required a technique of x-ray pelvimetry which will do two things. First, it must allow accurate measurement of all of the diameters desired. Second, it must show the true shape of the pelvis, particularly the inlet, so that the effect of shape upon the diameters can be determined. There are at

least twenty-three techniques which allow a reasonably accurate measure of the various diameters. The accuracy should be plus or minus 2 mm. Many techniques, however, although simple and accurate as far as measurement of the diameters is concerned, do not show the true shape of the inlet. It is therefore necessary to become more elaborate, and to use a method which shows the true shape of the inlet, either a positioning method or a stereoscopic method.

It has been usual for some years at the Sloane Hospital to use both the Caldwell-Moloy[1] and the Ball[2] method on each patient. Recently films have also been taken by the Colcher-Sussman[3] method and by the stereoscopic method with the patient positioned so that the inlet is parallel to the film. Since the x-ray studies of Caldwell and Moloy began at Sloane there have accumulated more than 8,000 cases of x-ray pelvimetry, and on the basis of this experience it is possible to state that there is no one single best technique. Study of these films led to the demonstration by Caldwell and Moloy that the shape of the pelvis exerts a strong influence on its capacity. In 1938 Moloy proposed that the capacity of the inlet might be measured by fitting a circle into the inlet as it was viewed in the stereoscope or on a flat film. A method of estimating disproportion based on this concept was subsequently described.[4]

The desirable technique of x-ray pelvimetry, then, will be one of several which will allow measurement of diameters and which will also allow a circle to be fitted to the inlet. Pelvic capacity can then be measured. The size of the fetal head can next be measured. Clinical estimation of the size of the fetus is notoriously misleading. It has been shown that while there is a general correlation between the size of the baby's head and the weight of the baby, the extremes of variation may be very large.[5, 6, 7] In the group of babies with a biparietal diameter of 9.5 to 9.9 cm., the smallest child weighed 1,900 grams and the largest weighed 5,000 grams. It becomes important to measure the size of the head. This can be done quite readily and with considerable accuracy in vertex presentations, although the breech presentation presents very real difficulties. The head may be measured in the precision stereoscope with a consistent accuracy of plus or minus 2 mm. However, the head can also be measured in the standing lateral film. The accuracy of examination in this film was pointed out by Rohan Williams,[8] who in a study of babies delivered by elective cesarean section, determined that the error in measurement of the head (except in those rare instances when the head was seen in a grossly distorted view) was the same as for the measurements of the pelvic diameters. Thus, in any simple technique which allows measurement of the pelvic diameters in the lateral view the head may also be measured. The size of the head may then be correlated with the size of the pelvic diameters and with the amount of space available as determined by the use of a circular form.

The time at which the films are obtained is also of some importance. The purpose of the films is to determine the relationship of the bony parts at the time of delivery, and the problem ought, therefore, to be studied as close to the time of delivery as possible. This means that most films are taken after the onset of labor. When films are taken before labor there are several disadvantages. First of all, the dates may be wrong, and a long time may elapse before labor occurs. It will then become necessary to take at least one more film to remeasure the size of the head. Second, the position of the head is often unfavorable before the onset of labor. Various attitudes are seen, many of which make measurement of the head questionable, so that a repeat film will be necessary subsequently. The only cases in which x-ray pelvimetry should be performed before the onset of labor are those in which the likelihood of elective cesarean section seems very large.

Details of Technique.—Standard x-ray equipment with a tube-film distance of 40 inches and a Potter-Bucky diaphragm with a 16:1 grid is used for the

standing anteroposterior and lateral films. This apparatus may also be used for stereoscopic films if precision stereoscopy by the Caldwell-Moloy method is not to be performed. If the Caldwell-Moloy method is used, it is necessary to use a tube-film distance of 25 inches and an 8:1 grid.

An anteroposterior film in the upright position is taken. A lateral film with the patient standing is next taken, the patient turning 90 degrees to her right from the position in which the anteroposterior film was taken. A metal ruler is placed between the buttocks for the lateral view.

The patient is then placed supine on the table, and a pair of stereoscopic views are taken, with a tube shift of 2½ inches, the target being centered at the level of the anterior superior iliac spines. When precision stereoscopy is to be carried out, the technique described by Moloy[1] is used.

When simple stereoscopy is desired, the cassette markers and the triangular markers are omitted, and any convenient tube-film distance is used. A triangular sponge rubber pad about 5 inches high is placed under the lumbosacral area. This causes the pelvis to flex backward into such a position that the inlet is parallel, or nearly parallel to the films. These films can then be viewed stereoscopically (although no measurements can be made in the stereoscope) or they can be viewed as flat films if desired.

A remark about stereoscopy is necessary at this point. It is important to view stereoscopic films in such a way that the distance from the eye to the film is the same as the distance from the target of the x-ray tube to the film at the time the films were taken. If different distances are used, a "stereoscopic" image can always be obtained, but this image will be distorted. The observer will not be aware of this distortion, for the image seems to be a good one. It was the accidental discovery of this fact which led to the development of the "precision stereoscope" with its close attention to detail. When precision stereoscopy is used, it is necessary to have the eye-film distance *exactly* the same as the tube-film distance, and the special markers used in the Caldwell-Moloy technique make this possible. But when ordinary stereoscopy is to be carried out it is necessary to have the eye-film distance within 3 cm. of the tube-film distance, otherwise the image of the pelvis will be distorted and misleading.

TABLE I. FORM FOR REPORTING PELVIMETRY FILMS

The senior house officer is responsible for this.
The following scheme should be used:

1. Give patient's name and x-ray number.
2. "X-ray pelvimetry reveals a . . . . . pelvis with the following measurements:
   - AP of inlet . . . . . cm.
   - Widest transverse of inlet . . . . . cm.
   - Circle of inlet . . . . . cm.
   - Interspinous diameter . . . . . cm.

   The diameter of the fetal head is . . . . . cm.
   The side walls are (straight, convergent, divergent).
   The sacrum is (straight, curved) and has a (forward, average, backward) inclination.
   The distance from the tip of the sacrum to the coronal plane through the spines is . . . . . cm.
   The subpubic arch is (wide, average, narrow).
   The fetus presents by the (vertex, breech, etc.) in the . . . . . position, with the leading part at . . . . . station.
   The difference at the inlet is . . . . . cm.
   The difference at the spines is . . . . . cm.
   This represents (no, borderline, absolute) disproportion.
   Report by Dr. . . . . .

This scheme may be varied as necessary, but the *pelvic type* and the *measurements* should always be given.

Method of Reading Films.—The anteroposterior and lateral films are examined in the standard viewing box. The stereoscopic films are examined in the stereoscope, or, when it is seen that the inlet is parallel to the film, one of the stereoscopic films can be examined as a flat film in the standard viewing box. The data are gathered according to a prepared work sheet (Table I). The films are first examined generally, all of the bony structures seen being checked for congenital or other anomalies, and for symmetry. The obstetrical presentation and position are noted. The type of the pelvis is determined according to the Caldwell-Moloy classification.

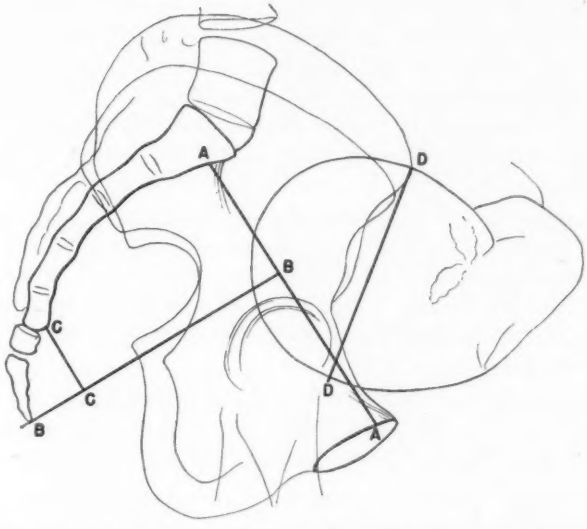

Fig. 1.—Method of measuring the standing lateral film.

Measurements are made as follows:

1. In the standing lateral film (Fig. 1):

   A. The anteroposterior diameter of the inlet is found by following the somewhat boat-shaped shadows produced by the flare of the ilia at the pelvic brim, and a line (*A-A*) is drawn at the level of the inlet from the posterior aspect of the symphysis to the anterior aspect of the sacrum. The promontory of the sacrum is seldom in the obstetrical inlet. The curve of the posterior part of the inlet generally sweeps into the first or second sacral vertebra. Anteriorly, the superior surface of the body of the pubis rises somewhat above the general level of the inlet proper, so that the anterior edge of the true inlet lies about 1 cm. below the top of the symphysis.

   B. The positions of the spines are marked, and a point midway between the spines is taken. A line (*B-B*) is then dropped through this point perpendicular to the line of the inlet, and extending caudad beyond the tip of the sacrum. This line represents the coronal plane through the spines. The intersection of this line and the line of the inlet (*A-A*) locates the position of the widest transverse diameter of the inlet.[9]

   C. A line (*C-C*) is then drawn from the tip of the sacrum, parallel to the line of the inlet, and intersecting the coronal plane through the spines.

   D. The fetal head is next examined (in vertex presentations) and a line (*D-D*) is drawn in the plane of the suboccipitobregmatic and biparietal

diameters. In 20 per cent of cases one or the other of these diameters will be clearly seen, the fetal head being found in the direct occipitoanterior, occipitoposterior, or occipitotransverse position. In 80 per cent of cases the head will be rotated to some extent away from these direct positions. In the great majority of cases, this rotation will be a simple one around the *long* axis of the head. In this event, the plane of the biparietal and suboccipitobregmatic diameters is readily recognized and measurement of the diameter as seen on the film is carried out. When the measurement of this diameter is compared with the actual value of the biparietal diameter it is found that the measured diameter is either equal to the biparietal or larger by not more than 3 mm. Occasionally the head is rotated in a more complex manner. In this event, it is not possible to identify the plane of the biparietal diameter, for the complex rotation brings an oblique frontooccipital diameter into profile. When this type of shadow is seen, measurement should not be carried out. Fortunately, this type of rotation is very rare when films are taken after the onset of labor.

The length of the anteroposterior diameter (*A-A*) and of the diameter of the fetal skull (*D-D*) are measured with a ruler. These measurements are then corrected by using the buttocks marker, which is marked in centimeters. Since these diameters are in the same plane as the marker, the distortion will be equal, and a simple count of centimeters will give the true diameter.

The length of the line *C-C* is measured directly on the film, and no correction is made. This distance is generally small, and variations of the amount introduced by correction are not clinically significant.

It should be noted that the position of the patient must be close to a pure lateral if measurements are to be made. With the tube centered at the left greater trochanter, a "perfect" lateral will result when the sacrosciatic notches are superimposed. If the peaks of these notches are more than 1 cm. apart the readings may be questioned, and if they are more than 2 cm. apart measurements should not be made.

2. The standing anteroposterior view (Fig. 2):

E. The widest transverse diameter of the inlet is drawn by inspection, *E-E*. The actual length of this diameter is then calculated according to the method described by Ball. This diameter lies at the point of intersection of the plane of the inlet and the coronal plane through the spines. This point is seen on the lateral film (intersection of *A* and *B*). The distance from this point to the outer margin of the sacral shadow is measured, along a line parallel to the posterior edge of the film. The outer margin of the sacrum represents the *anterior* face of the cassette holder, and the film is actually 4 cm. beyond this face. The distance from the point of intersection of lines *A* and *B* to the outer margin of the sacrum, plus 4 cm., represents the distance from the widest transverse diameter of the inlet to the film. Since the tube-film distance is already known, it is possible to set up an equation by which the true value of the diameter can be determined.*

*There are two aids to this calculation, the nomogram described by Ball,[2] and the special slide rule devised by Schwarz.[10] In addition, the use of a 40 inch tube film distance makes this very easy. This distance is 100 cm., nearly enough, so that the object-film distance at once allows a percentage to be established. Thus, if the distance from the widest transverse diameter to the outer shadow of the sacrum is 13 cm., and the depth of the film holder is 4 cm., the "object-film" distance will be 17 cm. The ratio of the true diameter to measured diameter according to the rule of similar triangles will then be 100-17/100, or 83/100, or 83 per cent.

F. The interspinous diameter, *F-F,* is then measured. The true value of this diameter is calculated by the same method described for the widest transverse diameter of the inlet, with the point between the spines on the lateral film used as the position of the interspinous diameter.

3. The stereoscopic films:

When the precision stereoscope is available, the anteroposterior diameter of the inlet, the widest transverse diameter of the inlet, the interspinous diameter, the circle of the inlet, and the diameter of the fetal head can all be determined by the method described by Moloy and Steer.[4]

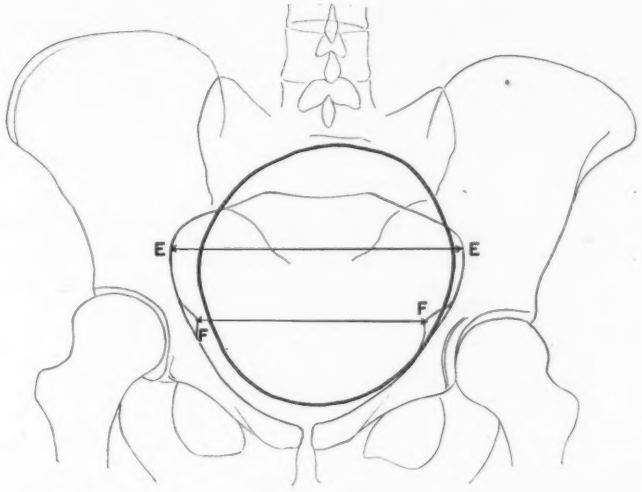

Fig. 2.—Method of measuring the standing anteroposterior film.

When the precision technique is not available, the stereoscopic films must be taken with the inlet parallel to the film, or a flat film should be taken with the inlet parallel to the film. The purpose of the stereoscopic or of this special flat film is to determine the influence of the shape of the pelvis upon the space available to the head. The simplest and most effective method of doing this is to place a circular disk (cut out of cardboard) in the inlet. This is done with great ease in a properly taken flat film, and the effect of shape is readily apparent (see Fig. 3). The actual size of this circle is equal to the anteroposterior diameter in gynecoid and flat pelves, but is smaller than this diameter in android and anthropoid pelves. When a circle is found which just fits the inlet, its true diameter can be readily calculated. The true anteroposterior diameter is already known from the lateral view. A ratio can then be set up as follows: measured AP diameter on "flat" film/true AP diameter = measured diameter of circle/true diameter of circle.

It is obvious that other techniques may be used to determine the true diameters listed above, but it is most important that the diameter of a circle which fits the inlet always be determined.

Estimation of Disproportion.—The possibility of disproportion is then estimated. The diameter of the head is subtracted from the diameter of the circle which fits the inlet. The numerical difference between these two diameters is called the "difference at the inlet," and this is the index of disproportion at this level.

The diameter of the head is next subtracted from the interspinous diameter. This number is the "difference at the spines." This produces an index of disproportion at the interspinous diameter, but this must be considered in relation to the amount of space before and behind the interspinous diameter. It is not possible to fit a circle into the plane of the spines. Two other factors are therefore considered here: the degree of forwardness of the sacrum* (line *C-C* in the lateral film), and the width of the subpubic arch.† A special film of the arch may be taken if desired, but the clinical description is adequate.

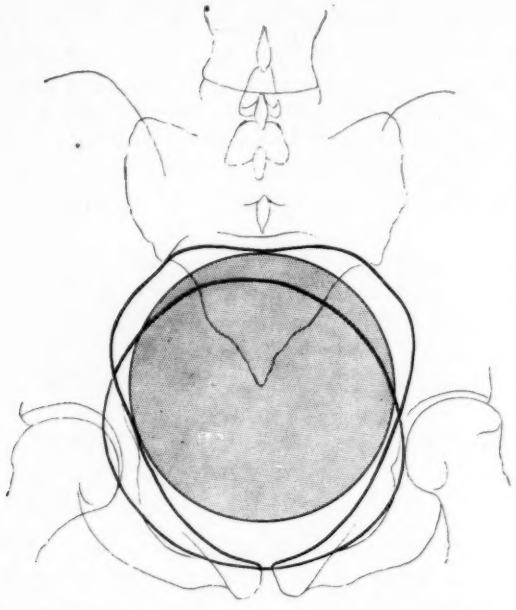

Fig. 3.—Method of placing a circle in the pelvic inlet.

Correlation of X-ray Prognosis With Outcome of Labor

In order to determine how accurately the outcome of labor may be forecast by means of x-ray pelvimetry, it is necessary to study only the cases in which an adequate trial of labor has been given. This excludes cases of elective cesarean section, and cesarean section performed with insufficient labor. It excludes cases of cesarean section or of forceps delivery performed because of uterine inertia, fetal distress, or other complications. The study group therefore includes all cases of spontaneous delivery, all of "elective" forceps, all of indicated forceps, and all cesarean sections performed after an adequate trial of labor.

*The forwardness of the sacrum: The measurement described above (line *C-C*) is the result of a number of attempts to measure the anteroposterior diameter at the level of the spines. The anterior rim of the plane through the spines extends out into space under the subpubic arch, the distance being a function of the arch. Measurements of the anteroposterior diameter from the sacrum to the arch have been made. Measurements from various points on the sacrum to the inferior aspect of the symphysis, and to the anterior end of the anteroposterior diameter of the inlet, have been made. These have been correlated with the outcome of labor by themselves. They have been related to the size of the head in various ways, and these results have been correlated with the outcome of labor. None of these correlations have worked out as well as the simple one of measuring the distance from the tip of the sacrum to the coronal plane through the spines.

†The subpubic arch: Measurement of the bituberous diameter, of the angle of the arch, of the depth of the arch (from the inferior aspect of the symphysis to the bituberous diameter) and of various combinations of these have been made. These have been correlated with the outcome of labor. The "measurement" which gives the best correlation is the simple description of the arch as "narrow" or "not narrow," and this description works as effectively when made by clinical examination as when made by x-ray.

Ideally, a trial of labor consists of full dilation of the cervix for 2 hours, with ruptured membranes and with good contractions. Practically, many patients do not reach this point, and therefore a trial of labor is defined as labor which finally results in cessation of progress as measured by the dilation of the cervix and descent of the head. There will be some difference of opinion as to the adequacy of a trial of labor under these conditions, but in each case those responsible for the clinical management of the patient were satisfied that an adequate trial had been given. Where there was any doubt, the case was not used.

Disproportion at the Inlet.—The material of this study is made up of 1,586 women in labor in the Sloane Hospital for Women, all of whom met the criteria previously described. The degree of disproportion at the inlet is expressed as the difference between the diameter of the circle which fits the inlet and the diameter of the fetal head. This difference is correlated with the outcome of labor according to the following groups: 1.0 cm. or less, 1.1 cm. to 1.4 cm., 1.5 cm. to 1.7 cm., and 1.8 cm. or greater. The results of this correlation are shown in Table II.

TABLE II. RELATION BETWEEN THE "DIFFERENCE AT THE INLET" AND THE OUTCOME OF LABOR

	DIFFERENCE AT INLET								
	1.0 CM. OR LESS		1.1 CM. TO 1.4 CM.		1.5 CM. TO 1.7 CM.		1.8 CM. TO MORE		
TYPE OF DELIVERY	NO.	%	NO.	%	NO.	%	NO.	%	TOTAL
Spontaneous	15	11	39	28	*72*	*38*	*422*	*39*	548
Low forceps	12	8	32	23	*64*	*34*	*627*	*55*	735
Midforceps	7	5	8	6	*28*	*15*	*48*	*4*	91
Cesarean section	107	76	62	43	*25*	*13*	*18*	*2*	212
Total	141		141		189		1,115		1,586

It is apparent that some patients (24 per cent) will be delivered from below even in the group with the highest degree of disproportion (difference 1.0 cm. or less). Such a high degree of disproportion can be overcome only by extreme degrees of molding, and this may be dangerous to the fetus. In 34 cases of delivery from below, 8 babies were lost because of laceration of the tentorium, a perinatal mortality of 24 per cent. In 107 deliveries by cesarean section, 2 babies were lost. One of these had had a trial at forceps, and died of a lacerated tentorium; and one died apparently of shock though no laceration of the tentorium was found.

It is also apparent that some patients will require cesarean section even when there is no disproportion at the inlet (difference 1.8 cm. or greater), because of disproportion below the inlet.

When the difference at the inlet was greater than 1.0 cm. there was no perinatal mortality due to the trial of labor, as long as no attempt at forceps delivery was made.

It is possible therefore to state the likelihood of delivery from below with any given degree of disproportion at the inlet, but it is not possible to state the prognosis absolutely in any individual case.

Disproportion in the Midpelvis.—The three indices of disproportion in the midpelvis are considered separately and together. The criterion for disproportion in this group is arrest in the midpelvis sufficient to warrant midforceps delivery or cesarean section. In recent years, cesarean section has been used more freely with midpelvic arrest, not because delivery from below is impossible but because the risk to the child is greater with a difficult forceps delivery than

with cesarean section. The method of delivery will necessarily vary from one case to another and under varying circumstances, but the important feature is that the head became arrested in the midpelvis.

The Difference at the Spines.—The difference between the interspinous diameter and the biparietal diameter of the fetus is correlated with the outcome of labor as shown in Table III. Since arrest in the midpelvis is treated by midforceps and by cesarean section, it is useful to compare the probability of these two types of delivery with that of spontaneous and low forceps delivery. When this is done, the "probability of serious arrest" is obtained. The table shows that the "probability of serious arrest" is 49 per cent when the difference at the spines is less than 0; 30 per cent when the difference is 0 to 1.0 cm.; and 8 per cent when the difference exceeds 1.0 cm.

TABLE III. RELATION BETWEEN THE "DIFFERENCE AT THE SPINES" AND THE OUTCOME OF LABOR

	DIFFERENCE AT SPINES						
	<0 CM.		0-1.0 CM.		>1 CM.		
TYPE OF DELIVERY	NO.	%	NO.	%	NO.	%	TOTAL
Spontaneous	27	29	*170*	*27*	*351*	*41*	548
Low forceps	21	22	*275*	*43*	*439*	*51*	735
Midforceps	9	10	*57*	*9*	*25*	*3*	91
Cesarean section	37	39	*134*	*21*	*41*	*5*	212
Total	94		636		856		1,586

It is significant that the probability of arrest is only 49 per cent even when the biparietal diameter is larger than the interspinous. This is so because of variations in the amount of space present in front of and behind the interspinous diameter itself.

The Distance From the Coronal Plane Through the Spines to the Tip of the Sacrum (CP → S).—This measurement (*C-C* in Fig. 1) is correlated with the outcome of labor in Table IV. When the incidence of midforceps is added to that of cesarean section, the "Probability of Serious Arrest" is seen to vary with CP → S as follows: CP → S less than 3.0 cm., probability of serious arrest 36 per cent; CP → S 3.0 to 4.5 cm., probability of serious arrest 24 per cent; CP → S greater than 4.5 cm., probability of serious arrest 10 per cent. This measurement, it must be noted, is considered as an independent one, *without* reference to the size of the head or the remainder of the pelvis. In arriving at the complete prognosis, these other factors must be considered also, as is shown below.

TABLE IV. RELATION BETWEEN THE DISTANCE FROM THE CORONAL PLANE THROUGH THE SPINES TO THE TIP OF THE SACRUM (CP → S) AND THE OUTCOME OF LABOR

	CP → S						
	<3.0 CM.		3.0-4.5 CM.		>4.5 CM.		
TYPE OF DELIVERY	NO.	%	NO.	%	NO.	%	TOTAL
Spontaneous	52	24	217	31	279	41	548
Low forceps	86	40	315	45	334	49	735
Midforceps	35	17	45	7	11	2	91
Cesarean section	40	19	116	17	56	8	212
Total	213		693		680		1,586

The Subpubic Arch.—The size of the subpubic arch is correlated with the outcome of labor in Table V. The probability of serious arrest is seen to vary as follows: subpubic arch narrow, probability of serious arrest 46 per cent;

subpubic arch average, probability of serious arrest 13 per cent; subpubic arch wide, probability of serious arrest 17 per cent. This measurement, like the preceding one, is also considered independently here, but in making the final prognosis all of the other features of the pelvis must be considered.

TABLE V. RELATION BETWEEN THE SIZE OF THE SUBPUBIC ARCH AND THE OUTCOME OF LABOR

	SUBPUBIC ARCH						
	NARROW		AVERAGE		WIDE		
TYPE OF DELIVERY	NO.	%	NO.	%	NO.	%	TOTAL
Spontaneous	43	15	411	39	94	38	548
Low forceps	116	39	506	48	113	45	735
Midforceps	28	10	47	5	16	7	91
Cesarean section	103	36	84	8	25	10	212
Total	290		1,048		248		1,586

The Midpelvis as a Whole.—In the preceding sections, it has been demonstrated that the probability of serious arrest is greatest when: (1) the difference at the spines is less than 0 cm. (probability 49 per cent), (2) the distance from the coronal plane through the spines to the tip of the sacrum is less than 3.0 cm. (probability 36 per cent), and (3) the subpubic arch is narrow (probability 46 per cent). A combination of all 3 of these factors represents the most severe degree of disproportion to be found in the midpelvis. This combination was found in 29 cases. Of these, *none* were delivered spontaneously; 10 required low forceps, 9 midforceps, and 10 cesarean section. The probability of serious arrest is therefore 65 per cent. However, there were 3 fetal deaths due to birth trauma in this group, 2 with low forceps and 1 with midforceps. The risk to the fetus in delivery from below with this type of disproportion is 3 in 19, or 16 per cent. These infants died of laceration of the tentorium. Descent of the head in this type of case occurs only when there is considerable molding, and the addition of a small amount of force will add enough molding to cause the tentorium to be torn.

Miscellaneous Types of Disproportion

1. Inlet Disproportion Alone.—There was disproportion at the inlet alone, without any evidence of disproportion in the lower pelvis, in 45 cases. The outcome of labor in these cases is shown in Table VI. The probability of serious arrest was 40 per cent.

TABLE VI. OUTCOME OF LABOR WITH DISPROPORTION PRESENT ONLY AT THE INLET

	DIFFERENCE AT INLET			
TYPE OF DELIVERY	1.0 CM. OR LESS	1.1 CM. TO 1.4 CM.	1.5 CM. TO 1.7 CM.	TOTAL
Spontaneous	3	7	3	13
Low forceps	1	5	8	14
Midforceps	1	5	6	12
Cesarean section	4	2	0	6
Total	9	19	17	45

2. Difference at the Spines 1 cm. or Less.—With no other evidence of disproportion, this occurred in 26 cases, in 9 of which delivery was spontaneous, 10 by low forceps, and 7 by midforceps. There were no cesarean sections. The probability of serious arrest was 27 per cent.

3. Inlet Disproportion, and a Difference at the Spines of 1 cm. or Less.—These were present in 58 cases, in 18 of which delivery was spontaneous, 15 by low forceps, 5 by midforceps, and 20 by cesarean section. The probability of serious arrest was 43 per cent.

4. Difference at the Spines of 1 cm. or Less, and CP → S 3.0 cm. or Less.—This occurred in 19 cases, 3 with spontaneous delivery, 9 by low forceps, 6 by midforceps, and one by cesarean section. The probability of serious arrest was 37 per cent.

5. Inlet Disproportion, Difference at the Spines of 1.0 cm. or Less, and CP → S 3.0 cm. or Less.—These were present in 19 cases, 4 with spontaneous delivery, 4 by low forceps, 2 by midforceps, and 9 by cesarean section. The probability of serious arrest was 58 per cent.

6. Difference at the Spines of 1.0 cm. or Less, and Subpubic Arch Narrow.—These were present in 17 cases, 3 with spontaneous delivery, 10 by low forceps, 3 by midforceps, and one by cesarean section. The probability of serious arrest was 24 per cent.

7. Difference at the Spines of 1 cm. or Less, Arch Narrow, and Inlet Disproportion.—These were present in 20 cases, 4 with spontaneous delivery, 3 by low forceps, one by midforceps, and 12 by cesarean section. The probability of serious arrest was 65 per cent.

8. Outlet Disproportion.—The pelvic outlet is formed by the ischial tuberosities and the tip of the sacrum. The tuberosities are never involved in bony arrest, because the head comes into contact with the descending rami of the pubes before it reaches the tuberosities in the cases in which the arch is narrowed. The tip of the sacrum *can* cause arrest in certain instances. Usually the forward tip of the sacrum is a part of generalized pelvic narrowing, so that the arrest is also caused in part by the spines and the descending rami of the pubes. There are cases, however, in which the entire pelvis is adequate except for a forward sacral tip, the head being held against the inferior aspect of the symphysis by the tip of the sacrum. These cases are rare, there being 8 in this series of 1,586. Delivery occurred spontaneously in one of these, by low forceps in 5, and by midforceps in 2. There were no cesarean sections.

9. The Narrow Subpubic Arch.—All of the features of the pelvis which can cause disproportion can be found occurring alone, except for the narrow subpubic arch. The arch is the easiest part of the pelvis to examine clinically, and it is highly significant that if the arch is found to be narrow there will always be additional features contributing to disproportion.

The Effect of Pelvic Type

The type of pelvis according to the Caldwell-Moloy classification is determined in all ward patients by clinical examination. It is possible to be certain of the pelvic type, of course, only by x-ray examination. The distribution of pelvic types found in the 5 year period 1950 through 1954 is shown in Table VII. The over-all distribution shows the pure gynecoid type to occur in the clinic population of the Sloane Hospital for Women in 73.6 per cent of cases, the android in 2.8 per cent, the anthropoid in 6.5 per cent, and the flat (or platypelloid) in 1.6 per cent. It is the rule to order an x-ray examination only when some possibility of disproportion is suspected clinically. In the years 1950 through 1954, x-rays were obtained on 9.5 per cent of the patients. The distribution of types determined by x-rays is of interest, for the patients found clinically to have gynecoid pelves were x-rayed in only 3.3 per cent of cases, while x-rays were obtained in 17 per cent of the android pelves, 21 per cent of the anthropoid pelves, and 34 per cent of the flat pelves.

The effect of the type of pelvis, regardless of the size of the fetus, is shown in Table VIII. The probability of serious arrest is given in all of the types of pelvis. Among the pure forms, whether typed clinically or by x-ray, trouble occurs with the gynecoid pelvis in 3.8 per cent, the anthropoid in 14 per cent, the flat in 24.2 per cent, and the android in 26.7 per cent.

The significance of the pelvic type, then, is to increase considerably the likelihood of serious arrest when the pelvis is of any type other than the pure gynecoid. Even with the ideal type, disproportion in its purest sense occurs in nearly 4 per cent of cases—that is, the pelvis is smaller than it should be

for a normal-sized child, or the child is larger than normal when the pelvis is of normal size. But distortion of the pure gynecoid form in any way increases the degree of disproportion, android characteristics being the worst in this respect, with platypelloid next, and anthropoid least.

TABLE VII. DISTRIBUTION OF PELVIC TYPES

TYPE OF PELVES	BY CLINICAL EXAM ONLY		BY X-RAYS		ALL CASES	
	NO.	%	NO.	%	NO.	%
Gynecoid	7,788	77.9	268	25.4	8,056	73.6
Gynecoid-android	377	3.8	56	5.3	433	3.9
Gynecoid-anthropoid	237	2.4	100	9.5	337	3.1
Gynecoid-flat	54	0.5	25	2.4	94	0.9
Android	256	2.5	53	5.0	309	2.8
Android-gynecoid	172	1.7	68	6.4	240	2.2
Android-anthropoid	29	0.3	36	3.4	65	0.6
Android-flat	3	0.03	17	1.6	20	0.2
Anthropoid	569	5.7	150	14.1	719	6.5
Anthropoid-gynecoid	117	1.2	54	5.1	171	1.5
Anthropoid-android	38	0.4	23	2.2	61	0.6
Flat	115	1.2	59	5.6	174	1.6
Flat-gynecoid	168	1.7	101	9.8	269	2.5
Flat-android	23	0.2	25	2.4	48	4.4
Rachitic	0	0	17	1.6	17	0.2
	9,946		1,052		11,013	

TABLE VIII. INFLUENCE OF PELVIC TYPE ON THE OUTCOME OF LABOR

TYPE OF PELVIS	TYPED BY X-RAY		PROBABILITY OF SERIOUS ARREST (%)
	TOTAL	CASES OF SERIOUS ARREST	
Gynecoid	268	15	5.6
Gynecoid-android	56	14	25.0
Gynecoid-anthropoid	100	24	24.0
Gynecoid-flat	25	3	12.0
Android	53	14	25.0
Android-gynecoid	68	25	36.8
Android-anthropoid	36	14	38.9
Android-flat	17	7	41.2
Anthropoid	150	43	28.7
Anthropoid-gynecoid	54	5	9.3
Anthropoid-android	23	3	13.0
Flat	59	14	23.7
Flat-gynecoid	101	22	22.0
Flat-android	25	14	56.0
Rachitic	17	3	17.6

Comment

A most determined effort has been made to discover whether the outcome of labor could be predicted in the individual case with a high degree of accuracy. In order to accomplish this, a detailed method of examining the pelvis and the fetal head was devised, and measurements were made with as careful a technique as possible, the usual error in measurement being not greater than plus or

minus 2 mm. Cases were chosen for study only when an adequate trial of labor had been given.* It is safe to say, therefore, that all possible information has been extracted from the films and that the cases are all satisfactory for testing.

It appears at once that a strictly accurate prognosis can never be given in the individual case from the x-rays alone, except in those extremely rare instances of gross pelvic distortion. When very high degrees of disproportion are present, some patients will still be delivered from below, because of great molding and powerful labor. When no disproportion is present some patients will still require operative delivery because of faulty position or attitude, or because of poor labor. What, then, can x-ray examination provide? It can provide a statistical statement of the probability of serious arrest in the individual case, and this can then be used as one factor in determining the best method of delivery. When one speaks of "accuracy" of x-ray prognosis, it is important to define the type of prognosis. If a "yes or no" prognosis is desired, x-rays are of no value. But if an accurate statistical prognosis is desired, the described method of x-ray study will provide it. The soundness of the figures stating the "probability of serious arrest" was tested by making this study in 3 steps. The first 350 cases were totaled, then another 300, and finally the remaining 986. The percentages in each subgroup agreed within 0.5 per cent, so that the figures for the entire group represent consistent findings.

The value of such prognostic data, then, is to allow a consideration of the entire case with a clear idea of what type of delivery will *probably* be necessary. These data will allow a recommendation of elective cesarean section only in one group—the group in which the difference at the inlet is 1.0 cm. or less. Even this recommendation is not based on the impossibility of delivery from below with this degree of disproportion, for 24 per cent of these patients will be delivered from below. It is based upon two facts: (1) that 76 per cent will require cesarean section, and (2) that the perinatal mortality in this group is 23 per cent when delivery does occur from below. Thus the x-ray findings even in this degree of disproportion are closely related to the clinical features of the case.

Since this is the only group of cases in which the x-ray finding is of paramount importance, all other cases should be given a trial of labor. The method of conducting this trial of labor will vary with the statistical prognosis as given by x-ray examination. A very long trial of labor will obviously not be carried out in the face of a high degree of disproportion. On the other hand, demonstration of the absence of disproportion will allow a long trial of labor and, if necessary, the use of drugs to stimulate the labor. Forceps delivery, when progress has stopped, can be carried out with a detailed description of the disproportion available, and cesarean section can be used instead of forceps when the degree of disproportion is demonstrated to be great.

The technique of x-ray pelvimetry is thus shown by this study to be an important aid in the management of labor, but, except for one very small

*This, together with some poor films, excluded 35 per cent of the cases x-rayed.

group of cases, it is not the prime factor upon which the decision as to type of delivery should be made.

Addendum.—All of the work here described refers to cases of vertex presentation. The question of disproportion in a breech presentation is a very real one, and it is necessary to state at this point that this question cannot be answered satisfactorily from the present study. First of all, the dangers of the breech presentation have long been known, and this group of cases was one of the first to be chosen for elective cesarean section when the slightest degree of disproportion was suspected. Since the studies of Caldwell and Moloy were begun in 1932, cases of trial of labor with questionable disproportion in a breech presentation have occurred only rarely. There are, consequently, too few cases upon which to determine a numerical expression of disproportion. Cases in which delivery occurred from below were almost invariably those of gynecoid pelves of normal or greater size. Now and then a patient is delivered from below when disproportion of a considerable degree is present, if we use the standards for disproportion derived from vertex presentations. Most of these deliveries have been difficult, but not all, and most of the babies have done well, but the numbers are too few to allow conclusions to be drawn.

There is a second drawback. All of the methods of determining head size in a breech presentation which we have tried have given an interesting and distressing type of error. It is possible to measure the head with an accuracy of plus or minus 2 mm. in 9 out of 10 cases. In one case in 10 the error may be as great as 2 cm. in the measurement of the biparietal diameter, but it is not possible to determine in which case the error occurs *until after the child is born.* This means that no reliance can be placed on the head measurement in a breech presentation, and hence no numerical expression of cephalopelvic disproportion can be made. This does not mean that x-rays should not be used, because the pelvis can be typed and measured accurately, and it is possible to determine how much space there is in the bony pelvis. When the amount of space is found to be ample for a child of average or larger size, delivery from below can be anticipated. When there is any evidence of disproportion, cesarean section is justified.

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THE SIGNIFICANCE OF THE UNENGAGED VERTEX IN A NULLIPARA AT THIRTY-EIGHT WEEKS' GESTATION

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ENGAGEMENT in a vertex presentation occurs, by definition, when the biparietal diameter of the fetal head passes the inlet. Although engagement is usually regarded as a phenomenon of labor, it has been taught that in a nullipara it frequently takes place during the last few weeks of pregnancy.[1] Indeed, it has been emphasized that one should be suspicious of cephalopelvic disproportion, if engagement has not occurred 2 weeks prior to term. Certainly, many obstetricians take a pessimistic attitude toward eventual vaginal delivery, if the fetal head is not engaged by the onset of labor.

It has been reported that clinical engagement in the nullipara occurs in over 90 per cent of cases at the onset of labor,[1, 2] but data on its frequency 2 weeks prior to the onset of labor are meager and the significance has not been studied by radiologic examination.

The present study was undertaken to determine the clinical significance of the lack of engagement in the nullipara at 38 weeks of gestation and at the onset of labor. When this study was well advanced, Buxton and Gordon[3] reported on a selected series of cases consisting only of nulliparas who showed x-ray evidence of lack of engagement at 38 weeks. We felt it was of sufficient interest to proceed with our study and compare the results.

Method

X-ray pelvimetry was performed on 250 consecutive nulliparas from the Obstetrical Clinic of the Beth Israel Hospital at 38 weeks of gestation. If engagement had not occurred, an additional standing lateral film was taken at the time when the patient entered the hospital in labor. We used the Torpin modification of Thoms's method of pelvimetry. The films were evaluated first by the radiology department (A. B.) and then reviewed by the obstetrical department (H. R. and L. B.). The pelvis was classified according to the method of Caldwell and Moloy.[5] The volumetric capacities of the inlet and midpelvis were analyzed by the method of Mengert.[4] Several cases were excluded from this analysis for technical reasons or because the films were not obtained at the proper date of gestation (thirty-eighth week). Thus 218 cases were available for analysis.

Results

A. Incidence.—At 38 weeks of gestation engagement had occurred in 163 cases (74.8 per cent) and had not occurred in 55 cases (25.2 per cent). This

corresponds to both Eastman's[1] clinical estimate of 75 per cent and the 70 per cent reported by Buxton and Gordon[3] (Table I).

TABLE I. NUMBER OF CASES SHOWING ENGAGEMENT BY X-RAY PELVIMETRY AT 38 WEEKS' GESTATION

	BUXTON AND GORDON 96 CASES		PRESENT SERIES 218 CASES	
	NO.	%	NO.	%
Engaged at 38 weeks	66	70	163	74.8
Unengaged at 38 weeks	30	30	55	25.2

Of the 55 patients without engagement at 38 weeks, engagement had occurred in 44 at the onset of labor. Thus the head was engaged in 207 cases (94.9 per cent) at the onset of labor and still unengaged in 11 cases (5.1 per cent).

B. Pelves.—In this series the incidence of the various types of pelves is shown in Table II. The distribution differs slightly from that reported by Moloy and Buxton and Gordon. Moloy reported 32.5 per cent and 23.5 per cent for android and anthropoid pelves, respectively, as compared to our 1.8 per cent and 12.8 per cent. Buxton and Gordon had 22 per cent android, as compared to our 1.8 per cent, and 4.4 per cent platypelloid, as compared to our 0.5 per cent. The mixed types were almost similar. We cannot account for this discrepancy in the distribution of types of pelves except by a difference in interpretation of minor variations in pelvic architecture.

TABLE II. VARIOUS TYPES OF PELVES

	ALL CASES		UNENGAGED AT 38 WEEKS		UNENGAGED AT ONSET OF LABOR	
	NO.	%	NO.	%	NO.	%
Gynecoid	126	57.8	30	23.8	7	5.6
Android	4	1.8	1	25.0	1	25.0
Anthropoid	28	12.8	7	25.0	1	3.7
Platypelloid	1	0.5	1	100.0	0	0.0
Gynecoid-android	43	19.7	12	27.9	1	2.3
Gynecoid-anthropoid	15	6.9	3	20.0	0	0.0
Android-anthropoid	1	0.5	1	100.0	1	100.0

Among the cases without engagement at 38 weeks, no one type of pelvis predominated. There was only one case in each of two categories, platypelloid and android-anthropoid, an incidence too small for statistical evaluation. In the cases in which engagement had not occurred at the onset of labor, the android and the android-anthropoid pelves had the highest incidence. In both categories again, however, the number of cases is too small for any statistical evaluation. Nevertheless, the trend as noted in these categories conforms with the teaching through the years, that the android pelvis, pure or mixed, is the poorest obstetrical pelvis.[7]

C. Mode of Delivery.—Table III shows the mode of delivery in this series. For statistical purposes, low forceps and spontaneous deliveries are grouped as "normal deliveries."

Of the patients in whom engagement had occurred at 38 weeks, 96.2 per cent had a "normal delivery." Two cases (1.2 per cent) were terminated by cesarean sections. This is in keeping with the hospital average.[6] Neither of the 2 sections was done for cephalopelvic disproportion. One was indicated for uterine inertia after 38 hours of labor in an adequate gynecoid pelvis and

the second was performed because of elderly primiparity after only 2 hours of labor. The latter patient had a gynecoid-anthropoid pelvis with adequate measurements. In the patients without engagement at 38 weeks, but with engagement at the onset of labor, 95.5 per cent had a "normal delivery." There were no cesarean sections. In 2 instances (4.5 per cent) midforceps were necessary. This is also in keeping with the hospital average. Of the 11 pregnancies without engagement at the onset of labor, 63.6 per cent were terminated by "normal deliveries." There were no midforceps deliveries. Four cases (36.4 per cent) came to cesarean section. In 3 there was definite cephalopelvic disproportion; one was a generally contracted pelvis with an 8½ pound baby; another was a contracted android pelvis with a 6 pound, 13 ounce baby; and the third was a gynecoid-android pelvis with adequate measurements and an 8 pound baby. The fourth patient, although having the diagnosis of cephalopelvic disproportion, probably had uterine inertia associated with possible cephalopelvic disproportion. This occurred in a gynecoid pelvis with adequate measurements and a 7 pound, 4 ounce baby. Despite 26 hours of labor, the vertex remained unengaged.

TABLE III. MODE OF DELIVERY

	ENGAGED AT 38 WEEKS		UNENGAGED AT 38 WEEKS, ENGAGED AT ONSET OF LABOR		UNENGAGED AT ONSET OF LABOR	
	NO.	%	NO.	%	NO.	%
Spontaneous delivery	30	18.4	16	36.4	2	45.5
Low forceps	127	77.8	26	59.1	5	18.1
Midforceps	4	2.4	2	4.5	0	0.0
Cesarean section	2	1.2	0	0.0	4	36.4
Total cases	163		44		11	

From the foregoing it is apparent that, if a vertex is engaged at the onset of labor, there is a 95 per cent chance of a "normal delivery," a 4 per cent chance of a midforceps delivery, and thus a 99 per cent chance of a pelvic delivery. If the vertex is unengaged at the onset of labor, only two types of delivery are to be anticipated, "normal" or cesarean section, the latter being probable in one-third of the cases.

D. Pelvic Capacities.—Mengert[4] uses an index to estimate inlet and midpelvic volumetric capacities by multiplication of the transverse and the anteroposterior diameters. He was able to compare a given pelvis with the average in terms of percentage. His figures showed that 85 per cent of normal capacity of either inlet or midplane represented the border line between adequacy and contraction. Table IV shows the capacities of the pelves calculated by Mengert's method in the various categories of engagement.

Of the 163 cases of engagement at 38 weeks, capacities of less than 85 per cent were found in only 3 cases (2 per cent) for the inlet and in 5 cases (3 per cent) for the midplane. In the cases without engagement at 38 weeks, but with engagement at the onset of labor, capacities of less than 85 per cent were found in 4 cases (9 per cent) both for inlet and midplane. Of the nulliparous patients in whom the vertex was unengaged at 38 weeks, approximately 10 per cent were found with a Mengert index of 85 per cent or less of the inlet or midplane, or both. Of the patients in whom the vertex was unengaged at the onset of labor, approximately 18 per cent had capacities of the inlet, midpelvis, or both, of 85 per cent or less.

In the first two categories, none of the patients with borderline capacities or below was subjected to cesarean section or midforceps. In the cases in

which the vertex was unengaged at the onset of labor, 2 of the 4 patients subjected to cesarean section had capacities below 85 per cent in either the inlet or midpelvis. One patient, however, with an inlet capacity of 79 per cent and a midpelvic capacity of 53 per cent, had a low forceps delivery of a 5 pound, 8½ ounce baby after 9 hours of labor in face presentation.

TABLE IV. VOLUMETRIC CAPACITIES OF THE PELVES

% CAPACITY	163 CASES OF ENGAGEMENT AT 38 WEEKS	44 CASES WITHOUT ENGAGEMENT AT 38 WEEKS BUT AT LABOR	11 CASES WITHOUT ENGAGEMENT AT ONSET OF LABOR
Inlet.—			
96-100+	142	31	4
91-95	14	6	0
86-90	4	3	5
81-85	3	2	1
76-80	0	2	0
71-75	0	0	1
Midpelvis.—			
96-100+	134	28	7
91-95	15	7	0
86-90	9	5	2
81-85	2	4	1
76-80	3	0	0
71-75	0	0	1

Summary

1. Two hundred and fifty consecutive nulliparas were subjected to x-ray pelvimetry at 38 weeks of gestation. If there was failure of engagement, an additional standing lateral film was taken on admission to the hospital at the onset of labor. Two hundred and eighteen cases were available for analysis.

2. Engagement had occurred in 74.8 per cent at 38 weeks and had not occurred in 25.2 per cent.

3. Of the patients without engagement at 38 weeks, engagement had occurred in 80 per cent at the onset of labor. The vertex was engaged in 94.9 per cent of all cases at the onset of labor and was still not engaged in 5.1 per cent.

4. The distribution of the types of pelves found in this series was very similar to that given in other reports except for a smaller number of android and anthropoid pelves.

5. The android pelvis, pure or mixed, was implicated most often in the failure of engagement at the onset of labor.

6. If the vertex is engaged at the onset of labor, 99 per cent will have a pelvic delivery. If it is unengaged at the onset of labor, 63.6 per cent will have pelvic delivery and 36.4 per cent will require cesarean section.

Conclusions

1. In 75 per cent of nulliparas with the vertex presenting, engagement has occurred at 38 weeks.

2. In 95 per cent of nulliparas with the vertex presenting, engagement has occurred at the onset of labor.

3. If the vertex is engaged at the onset of labor, pelvic delivery can be anticipated in 99 per cent of the cases.

4. If the vertex is unengaged at the onset of labor, the need for cesarean section can be anticipated in 36 per cent of the cases.

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THE OBSTETRIC RISK OF THE JAPANESE WOMAN WITH A CAUCASIAN HUSBAND

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THE effects of interracial marriages have long been an interesting source of speculation to the geneticist and the obstetrician. Engelmann,[1] following his studies among the American Indians, felt that the problem of dystocia might well be a consequence of intermarriage among people of different races and skeletal types. Mack[2] recently brought this speculation to our attention when he discussed the journals of Lewis and Clark in his presidential address before the Central Association of Obstetricians and Gynecologists. He suggested that ". . . the American melting pot, continues to beget disproportion."

Since World War II, the military hospitals in the Orient have been confronted with the obstetric management and delivery of the "petite" Japanese woman married to a "giant" American Caucasian. This problem, however, is no longer limited to military medicine in Japan. With the rotation of the serviceman and his family and his separation from the Armed Forces, these families have been disseminated throughout the United States and affect military and civilian practices alike. The new Armed Forces Medical Care Act has helped to speed the extension of this situation to civilian practice. The scope of the problem may better be realized when it is seen that during the period from Sept. 2, 1945, through June 30, 1956, 26,101 Japanese women married United States citizens stationed in Japan.

At the time of arrival of the senior author in the Far East in September, 1954, many of the practicing obstetricians in the military services were of the general opinion that the Japanese female possessed internal pelvic measurements far below those of the average Caucasian and that intermarriage to an American husband rendered her an obstetric risk. Others felt that this was not true and that these patients possessed adequate pelvic measurements and were satisfactory obstetric risks.

For these reasons, at Tokyo U. S. Army Hospital, a standard method of internal pelvimetry was instituted and a survey started for evaluation of this problem.

In July, 1956, a total of 500 charts of these Japanese women who were delivered of term infants fathered by Americans were withdrawn from the hospital files for computation. These patients were not necessarily delivered

consecutively and were selected at random by the registrar staff from a total of some 700 deliveries falling into this interracial category. The only criterion specified for selection was that the infant's weight should equal or exceed 2,500 grams. During the period selected from September, 1954, through June, 1956, 41.71 per cent of the total deliveries were Japanese-American.

For comparison, 500 charts of Caucasian women were similarly procured from the registrar's files, with the only specification again that the weight of the infant should equal or exceed 2,500 grams. These patients were delivered during relatively the same period of time and by the same obstetric staff.

Findings

General Labor and Delivery Pattern.—The obstetric analgesia, anesthesia, and type of delivery followed an identical prescribed pattern in both groups of patients. Analgesic agents were Demerol (100 mg.) and Seconal (0.1 Gm.) in early labor and self-administered Trilene for late labor. Approximately 96 per cent of both groups received Nupercaine (2.5 mg.) saddle block anesthesia. Pudendal or local anesthesia with 2 per cent procaine was substituted in the cases in which time did not allow for the routine saddle block or in which the latter was felt not advisable. Spinal Pontocaine anesthesia was utilized for cesarean sections. The routinely practiced delivery method was by low forceps over a wide mediolateral episiotomy. Approximately 88 per cent of the patients in both groups were delivered by this method and there were no significant variations between the groups for breech extractions, midforceps, or spontaneous deliveries. The cesarean section rate was identical in both groups, 1.0 per cent, or 5 cases. In each group there were 3 primary and 2 "repeat" cesarean sections. In the Japanese, only one of the primary sections was for cephalopelvic disproportion. None of the primary sections in the Caucasian series was for this indication.

Physical Data on Patients.—

Age: The average age of the Japanese patients was 25.23 years as compared with 27.40 years for the Caucasian patients.

Height: The heights were recorded only for the Japanese and the average was found to be 60.9 inches.

Weight: This was also computed for the Japanese only and the average was 107.29 pounds.

Gravidity and parity: The gravidity and parity, including abortions, of both groups are as listed in Tables I, II, and III.

TABLE I. GRAVIDITY

	I	II	III	IV	V	VI	VII	VIII	IX	XVIII
Japanese	33.6%	43.6%	17.4%	3.2%	1.8%	0.2%			0.2%	
Caucasian	25.2%	28.6%	24.4%	9.0%	7.4%	3.2%	1.2%	0.6%	0.2%	0.2%

TABLE II. PARITY

	NONE	I	II	III	IV	V	VI	IX
Japanese	62.0%	28.2%	7.6%	1.8%	0.4%			
Caucasian	28.4%	32.6%	22.4%	9.8%	4.8%	1.0%	0.8%	0.2%

TABLE III. ABORTIONS

	NONE	I	II OR MORE
Japanese	59.8%	33.4%	6.8%
Caucasian	82.2%	11.4%	6.4%

Pelvic measurements: Clinical mensuration was performed on all patients in both groups. X-ray pelvimetry was utilized only as felt indicated. Measurements for the Caucasian women were not actually computed for this study but a general survey confirmed them to be fairly consistent with those already reported in numerous articles and texts.

The bony pelvis of the Japanese woman was found to be remarkably consistent and surprisingly adequate when considering the small pelvic girth. Over 95 per cent were as described in Table IV.

TABLE IV. GENERAL CHARACTERISTICS OF THE JAPANESE PELVIS

Pubic arch	90°
Biischial diameter	9.0 cm.
Diagonal conjugate	12.5 cm.
Posterior sagittal diameter	9.0 cm.
Coccyx	Movable, light structure
Sacrum	Gynecoid curve
Ischial spines	Blunt, small
Fore pelvis	Ample, rounded
Type of pelvis	Gynecoid

Length of labor: In calculating the length of labor, the mean or average lengths were used. In this, as in most series, extremes were not common but did occur. The shortest length of labor was 30 minutes and the longest 43 hours.

TABLE V. LENGTH OF LABOR

	OVER-ALL AVERAGE	PRIMIPARAS	MULTIPARAS
Japanese	7 hours, 37 minutes	8 hours, 42 minutes	5 hours, 23 minutes
Caucasian	6 hours, 46 minutes	9 hours, 43 minutes	5 hours, 36 minutes

Weight and Length of Infants.—The weight and length of the infants were likewise calculated on the mean or average. Extremes in weight were not common but varied from a minimum of 2,500 grams in both groups to a maximum of 4,479 grams in the Japanese and 4,876 grams in the Caucasian. Variations in length in both groups were minimal. The shortest infant in both groups was 43.18 cm., while the longest was 55.88 cm. for the mixed-blood infant and 57.15 cm. for the Caucasian.

TABLE VI. WEIGHT AND LENGTH OF INFANTS

	AVERAGE WEIGHT	AVERAGE LENGTH
Japanese	3,199 grams	50.16 cm.
Caucasian	3,354 grams	51.08 cm.

Morbidity and Mortality.—There was no maternal death. The usual maternal morbidity, including toxemia, lacerations, placental mishaps, cystitis, pyelitis, mastitis, and episiotomy separations and infections, was virtually identical in the two racial categories. The exception to this was the relatively large number of cases of active tuberculosis in the Japanese women despite the rigid premarital examination requirements. In the 500 deliveries of Japanese women reviewed, there were 11 cases of tuberculosis. All of these patients were delivered without incident.

The infant morbidity and mortality likewise exhibited no variations of statistical significance between the Japanese-Caucasian and Caucasian.

Comment

The wide variation between gravidity and parity in the Japanese women was felt to be of interest (Tables I and II). While 62.0 per cent were nulliparous, only 33.6 per cent were undergoing their first pregnancy as compared

to 25.2 per cent and 28.4 per cent, respectively, for the Caucasian women. This variation is readily explained by the liberal indications for induced abortion in Japan. Pommerenke[3] in his account of abortions in Japan, which he compiled as visiting professor in his General Report to the Unitarian Service Committee, covered very thoroughly the Japanese attitude and available statistics on this subject. Of the total of 40.2 per cent who had had abortions, 74.1 per cent admitted one or more induced abortions (Table III). No induced abortions were acknowledged by the Caucasian group.

In spite of the small pelvic measurements reported by some physicians, this was not confirmed in the Japanese women examined in this series or by this hospital staff. In general, the pelves were found to be true gynecoid in type with over 95 per cent of the type described in Table IV. Because of the large number of referrals and transfers, opportunity was presented to examine many patients listed by others as having small or inadequate measurements. Re-evaluation showed the great majority of these to be a result of faulty mensuration.

Although a retrospective process, there can be no better evaluation of any patient as an obstetric risk, including adequacy of the pelvis, than the comparison of the length of labor with the size of the fetus. Tables V and VI list these comparative factors for the two groups in this series. The minor variation between the Japanese and Caucasians in length of labor was felt to be without significance. Although the over-all length of labor for the Japanese women was approximately one hour longer than for Caucasians, the over-all length of labor for the Japanese primiparas was one hour less. We feel that these figures are justifiably comparable because of the identical management and criteria for determining labor used in each patient. Table V appears to represent a discrepancy whereby both primiparous and multiparous Caucasians had longer average labors than comparable Japanese women, yet the Caucasians exhibited a shorter over-all average. This is readily understandable by reference to Table II, which shows that 62.0 per cent of the Japanese were primiparas as compared to 28.4 per cent for the Caucasians.

The weight and length of the infants were found likewise to exhibit an almost negligible variation. This showed the infants delivered of Japanese women to be only 155 grams and 0.92 cm. less than those delivered of the Caucasian women. The higher degree of multiparity among the Caucasians might be expected to explain these differences without reference to the small size of the Japanese race. Although fetal head measurements were not recorded, a general survey of the infants delivered in the two groups showed no appreciable difference and the measurements were consistent with those generally reported for the Caucasian race.

Summary

A series of 500 deliveries of Japanese women married to Caucasians, compared with a similar series of deliveries of Caucasian women, has been reviewed and presented with the view of determining the obstetric risk in the mixed marriages between the smaller statured Japanese women and the Caucasian men.

Although the series was small, it is felt that the findings are significant and comparable because of the identical management and criteria utilized.

The Japanese woman married to a Caucasian was found to present no greater difficulties in obstetric management than her Caucasian counterpart.

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A COMPARISON OF OXYTOCIC DRUGS IN THE MANAGEMENT OF THE PLACENTAL STAGE*

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THE use of an oxytocic drug in the management of the placental stage is widespread in modern American obstetrics. While the type of oxytocic drug, the method, and the time of injection vary, the prime object is to decrease the blood loss with the delivery of the placenta. This is to ensure a contracted uterus until the normal uterine retraction and thrombosis in the maternal sinuses occur, thereby lessening the incidence of postpartum hemorrhage which is still one of the leading causes of maternal mortality.

For the past twenty-odd years, ergonovine, a purified alkaloid of ergot, and solutions of posterior pituitary, which have been used for over forty years, have been the oxytocic agents in most general use. Because of the pressor and antidiuretic components of the whole pituitary extract, the oxytocic portion, Pitocin, has usually been used, thereby decreasing untoward reactions, although it too, contains a small amount of the pressor and antidiuretic hormones. Ergonovine and Pitocin have proved highly efficacious as oxytocic agents, the pituitary extract acting slightly more rapidly but not having as prolonged an action as ergonovine. Because of the scarcity of supply and high cost of production, of both substances, however, the search has continued to find an oxytocic agent which can be produced at a lower cost and will cause fewer undesirable reactions. Davis and associates[1] reported that there were no systemic reactions following the use of intravenous or subcutaneous ergonovine, but subsequent studies by Dieckmann and co-workers[2] and others have shown that increases in blood pressure, etc., do occur.

Material and Methods

The synthetic compounds used in this study were alpha, alpha diphenyl gamma dimethylamino N-methyl valeramide-HCl (Upjohn U3772) and Syntocinon (Sandoz), a synthetic oxytocic principle of the posterior pituitary. These two compounds as well as ergonovine and Pitocin were packaged in identical manner in single-dose vials and were administered intravenously in rotation to the patients being delivered on the staff services. The oxytocic agent was identified only by a number which was meaningless to the obstetrician in charge of the case.

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†Deceased.

The procedure was as follows: Two milliliters of the unknown drug was administered intravenously when the anterior shoulder of the fetus was visible beneath the symphysis. The delivery was completed slowly after a 30 second interval to allow the oxytocic agent to exert its effect. The time interval between delivery of the baby and separation of the placenta was noted. The method of delivery of the placenta was recorded. The blood lost when the placenta separated was collected in a basin containing 200 ml. of 4 per cent sodium oxalate solution as an anticoagulant, and was measured in a graduated cylinder. Additional information concerning the delivery was recorded. This included the age and gravidity of the patient, the analgesic and anesthetic drugs used in the labor and delivery, the total length of labor, and the birth weight of the infant. Any abnormalities of presentation were recorded. In addition, blood pressures were observed and idiosyncrasies to the oxytocic agent were watched for.

In 28 cases the blood collected with separation of the placenta was combined with that absorbed by the vaginal packing used during repair of the episiotomy and perineal pads for a period of one hour post partum and measured accurately, by the hemoglobin method.

In another series, 14 patients were given one of the four oxytocics intravenously on one occasion during the postpartum period up to the ninth day. Blood pressure, pulse, and evidence of idiosyncrasies were recorded before, immediately after, and at 5 minute intervals for 30 minutes following administration. This was done to observe the effects of the tested drugs without the presence of analgesic or anesthetic agents which might alter the response.

In addition, 8 postpartum patients known to be free of cardiac lesions were subjected to electrocardiographic tracings before and after the intravenous administration of the drugs studied.

In 8 cases the infant was delivered without administration of the oxytocic drug. The placenta was removed manually immediately and a rubber bag was inserted into the uterine cavity. This was filled with 200 ml. of sterile water and held in place with a vaginal pack. The inflated bag was connected to a kymograph and tracings of uterine contractions recorded before and after the administration of the oxytocic drug.

Throughout the study the drugs were injected intravenously and the dosage used was as follows: ergonovine, 4 mg.; Pitocin, 2 I.U.; Syntocinon, 2 I.U.; and U3772, 80 mg.

A total of 624 deliveries were studied. Ergotrate was used in 149 patients; 168 patients received Pitocin; 156 were given Syntocinon, and 151 received U3772. The total length of labor did not vary significantly from group to group. Less than 1 per cent of labors were longer than 24 hours with the exception of those of the group who received ergotrate as the oxytocic agent. This is pure chance and if the sampling were larger this apparent difference in the groups would undoubtedly disappear. The length of labor in over 50 per cent of all the cases studied was less than 8 hours (Table I).

TABLE I. LENGTH OF LABORS

TOTAL LENGTH OF LABOR (HOURS)	% OF CASES			
	ERGOTRATE	PITOCIN	SYNTOCINON	U3772
Less than 2	9.0	7.7	8.5	7.3
2-4	11.9	23.1	27.5	21.9
4-8	41.8	35.3	37.3	38.4
8-16	28.4	28.8	23.9	31.8
16-24	6.0	4.5	2.8	0.0
24+	3.0	0.6	0.0	0.7

The analgesic drugs used varied, depending upon the preference of the obstetrician in charge. Generally sedation was given only once with one of the following agents: morphine, 10 mg.; Demerol, 100 mg.; methadone, 5 or 10 mg. Approximately 50 per cent of the patients in each group received no analgesic whatsoever. A small percentage of each group were given inhalation analgesia in the form of ethylene-oxygen mixtures with contractions (Table II).

TABLE II. ANALGESIC AGENTS USED

ANALGESIA EMPLOYED	% OF CASES			
	ERGOTRATE	PITOCIN	SYNTOCINON	U3772
Morphine and scopolamine	25.7	18.9	20.3	19.0
Demerol and scopolamine	14.0	11.6	14.9	14.1
Methadon and scopolamine	8.8	4.9	7.4	11.7
Atropine	0.0	1.2	0.0	0.0
Nothing	47.1	56.7	51.3	48.5
Gas with pains	4.4	6.7	6.1	6.7

Anesthetics varied but the distribution was approximately the same for each of the oxytocics used. Over 50 per cent of each group received saddle block anesthesia with Nupercaine. The patients were in the second stage of labor before the spinal anesthetics were given. We have found that the employment of this anesthesia during the first stage of labor is hazardous since a fall in blood pressure can be dangerous to the fetus. Over 80 per cent of the deliveries were carried out under saddle block or ethylene-oxygen anesthesia. The remainder of the patients were given cyclopropane-oxygen, local, or open drop ether anesthesia. Less than 2 per cent of any group received no anesthetic agent for delivery (Table III).

TABLE III. ANESTHESIA USED

ANESTHESIA	% OF CASES			
	ERGOTRATE	PITOCIN	SYNTOCINON	U3772
Saddle block	65.7	62.5	59.0	62.2
Ethylene and oxygen	20.0	19.0	23.1	25.0
Ethylene, ether, and oxygen	8.6	10.7	10.9	6.4
Cyclopropane and oxygen	0.0	0.0	1.3	0.6
Ether	2.1	1.2	1.3	0.0
Nothing	0.7	1.8	1.9	1.2
Local	2.9	4.8	2.6	4.7

TABLE IV. METHOD OF DELIVERY OF THE PLACENTA

METHOD	% OF CASES			
	ERGOTRATE	PITOCIN	SYNTOCINON	U3772
Prompt expression	72.1	78.4	76.9	71.3
Shoehorn	3.7	6.2	4.5	7.2
Manual	24.3	15.4	18.6	21.6

The method of delivery of the placenta did not vary with the different oxytocic agents (Table IV). Over 70 per cent were delivered spontaneously and promptly after administration of the oxytocic. The unusually high percentage of manual removals is due to the fact that the vast majority of these were done for teaching purposes. It is the practice in our institution to train residents in this procedure. Thus, any placenta which cannot be expressed within 10 minutes without hemorrhage would be removed manually, and, if there were hemorrhage, immediately. The shoehorn method is carried out when the placenta is protruding through the cervix and it is gently delivered by traction.

Results

The time of delivery of the placenta was not significantly different in the various groups. Over 60 per cent of the placentas were delivered spontaneously within 3 minutes after administration of the oxytocics in all groups. The longest period for the delivery of the placenta was 9 minutes, which occurred in 5 per cent of cases or less in the various groups (Table V).

TABLE V. TIME OF DELIVERY OF PLACENTA AFTER OXYTOCIC

TIME IN MINUTES	% OF CASES			
	ERGOTRATE	PITOCIN	SYNTOCINON	U3772
1	14.4	15.5	10.6	14.0
2	26.6	26.7	28.5	27.9
3	17.3	24.2	23.8	15.7
4	12.9	12.4	15.9	13.4
5	7.2	9.9	10.6	11.0
6	7.2	3.7	7.3	7.6
7	5.8	3.1	0.7	4.1
8	3.6	0.6	0.0	1.7
9	5.0	3.7	2.6	4.7

Table VI shows the blood loss with the placenta, as measured in a graduate by the resident in charge. In 70 per cent of the cases where U3772 was used and 80 per cent or more with the other three oxytocics, the blood loss was less than 100 ml. A very small percentage of the patients had blood losses in excess of 200 ml. Syntocinon seemed a little more effective in reducing blood loss than Pitocin or ergotrate. Dieckmann and his associates[3] measured the blood loss at delivery as determined by the residents and found the data listed in Table VII. Where the blood loss was exactly determined as hemoglobin, these values were comparable to those reported by us (Table VII).

TABLE VI. MEASURED BLOOD LOSS WITH PLACENTA

BLOOD LOSS (C.C.)	% OF CASES			
	ERGOTRATE	PITOCIN	SYNTOCINON	U3772
0-25	54.6	44.2	56.1	41.1
26-99	26.9	37.2	24.3	29.7
100-199	15.4	16.0	16.9	23.4
200-299	3.1	2.6	0.7	1.9
300-499	0.0	0.0	0.0	3.8
500+	0.0	0.0	0.0	0.0

TABLE VII. BLOOD LOSS WITH PLACENTA AND FOR ONE HOUR POST PARTUM

AFTER DELIVERY OF ANTERIOR SHOULDER						
DIECKMANN'S STUDY			PRESENT STUDY			
SODIUM CHLORIDE SOLUTION	ERGONOVINE 0.2 MG.	POSTERIOR PITUITARY 2 U.	ERGONOVINE 0.4 MG.	PITOCIN 2 U.	SYNTOCINON 2 U.	U3772 80 MG.
192 ml.	86 ml.	63 ml.	40.8 ml.	59.3 ml.	40.3 ml.	81.8 ml.

When the blood loss was measured during delivery of the placenta, it tended to be slightly greater when U3772 was used as the oxytocic agent. This tendency is even more pronounced than appears in the data presented because not infrequently with the use of this drug uterine relaxation occurred

within a 10 or 15 minute interval following delivery. This phenomenon was further verified by the more accurate determination of blood loss with the placenta and for one hour post partum by the hemoglobin method (Table VII).

When the patients were given the oxytocic agent on various postpartum days no significant change in blood pressure or pulse could be elicited. Electrocardiograms taken before and after administration of the oxytocic showed no change. Patients complained of few subjective symptoms. With ergotrate, Pitocin, and Syntocinon the universal response was uterine cramping. This was more pronounced soon after delivery than later in the postpartum period. The uteri appeared to be more responsive to the action of the oxytocic on the first day post partum than on the seventh day following delivery. The patients who received U3772 all stated that they experienced a feeling of "heat" in the throat and abdomen. This was transient and no other subjective symptoms were elicited. Kymographic tracings obtained with the intrauterine bag demonstrated typical tonic contractions on which were superimposed clonic contractions following the injection of the oxytocic drug.

Comment

An effective oxytocic drug is part of the desirable armamentarium of every obstetrician. A constant search is being conducted for better therapeutic agents. The ideal oxytocic for the placental stage would be a drug which would produce no untoward systemic reactions, cause the uterus to remain contracted, and lower the incidence of postpartum hemorrhage. No drug which is therapeutically active is completely safe and no oxytocic drug can absolutely prevent the occurrence of postpartum hemorrhage. It is impossible for the uterus to remain tetanically contracted; if it did, it would become gangrenous.

Ergonovine, since its introduction in the management of the placental stage more than twenty years ago, has seemed to be an ideal drug when given in an adequate amount, which we think is 0.4 mg. or more intravenously. It is rather costly and difficult to obtain, however, since every batch of ergot does not contain sufficient ergonovine to warrant extraction. Solutions of posterior pituitary or Pitocin from animal sources contain some foreign protein and, although the number of patients who are sensitive to this protein is very small, it is potentially dangerous. Furthermore, the supply is dependent upon the slaughterhouse. We have had one patient in over 150,000 deliveries who was sensitive to an intradermal wheal of solution of posterior pituitary diluted 1 to 1,000. With the synthesis of the oxytocic fraction of the posterior pituitary gland, there should be less possibility of anaphylaxis. Furthermore, the manufacturer is not dependent on any foreign product such as ergot or on the slaughterhouse for his basic material.

The compounds reported upon in this investigation have demonstrated that there is no significant improvement in the physiological action of Syntocinon, the synthetic posterior pituitary hormone, over ergotrate and Pitocin. The great advantage of this compound over the naturally occurring posterior pituitary hormone, however, is that it is a synthetic substance not dependent on biological sources for its manufacture and it is not contaminated by other pituitary factors such as the antidiuretic or pressor hormones.

On the other hand, U3772 is not an effective oxytocic clinically. Its duration of action is in many cases too transient to be effective as a hemostatic agent. Clinically it has not proved to be as effective an oxytocic agent as ergotrate, Pitocin, or Syntocinon.

Summary and Conclusions

The effectiveness of Syntocinon as an oxytocic agent has been demonstrated. Its activity in this respect is indistinguishable from that of the

naturally occurring oxytocic principle of the posterior pituitary. It is effective in preventing postpartum atony and consequently in reducing blood loss with the placental stage of labor. It is a clinically effective oxytocic agent.

On the other hand, U3772 is not as effective an oxytocic agent as ergonovine, Pitocin, or Syntocinon for clinical use. Its action is too transient and not dependable in the dosage employed.

No idiosyncrasies were encountered with any of the drugs used, with the exception of a feeling of "heat" in patients without analgesia or anesthesia when U3772 was used.

No significant changes in blood pressure, pulse, or electrocardiographic tracings were encountered with any drug.

When the drugs were administered with an intrauterine balloon in place, all demonstrated oxytocic effects.

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PROMETHAZINE AS AN ADJUNCT TO OBSTETRICAL ANALGESIA AND SEDATION

A Series of 500 Cases

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THE majority of obstetricians feel that analgesia and sedation are indicated during labor, but routine measures for relief of the patient's pain are generally inadequate and dangerous to the infant.

Grantly Dick Read's writings[1, 2, 3] have revived interest in the psychological aspects of pregnancy and parturition, about which, even yet, very little is known.[4] His method involves a system of prenatal indoctrination and a regimen of muscular exercises designed to ally the apprehension of the patient and aid her in achieving voluntary physical relaxation during labor.

Prenatal Indoctrination.—In this study we have incorporated some of Read's prenatal indoctrination, and have employed a different method of obtaining analgesia and sedation during labor. We have attempted to decrease the dosage of respiratory depressant drugs used and, at the same time, obtain what we consider safe and adequate analgesia and sedation with no detrimental effect upon the patient or infant.

Simple psychotherapy should be practiced as part of the prenatal program from the earliest visit to the physician. During pregnancy our patients make approximately 12 to 14 visits to our office, or more if advisable. At each visit, after the routine examination has been completed, the patient returns from the examining room to the private office for a talk with her obstetrician. This verbal contact with the patient does more to establish rapport and dismiss the fearful unknowns of pregnancy than sending her home armed with printed literature only.

We make every effort to nurture in the patient a will to conscious participation in the birth process. The risk to the infant of respiratory embarrassment from narcotics is stressed, as well as the fact that by insisting on delivery in the unconscious state she is depriving herself of a profound experience to which she has a natural right. She is assured, however, that medication will be provided to relieve the most painful and exhausting phases, although a certain amount of discomfort cannot safely be avoided.

Sedation and Analgesia.—In our practice the results obtained with meperidine and scopolamine in the dosages usually employed have coincided with the experiences of many others. Especially in the conduct of prolonged or severe labor or in association with a general anesthetic for delivery, the well-known depressant effects have been a handicap.

Earlier descriptions of the ataractic compounds[5, 6, 7] stimulated us to investigate the possible usefulness of certain of these agents during labor. Chlorpromazine, a chlorinated derivative of phenothiazine, has been advocated by some authors.[8, 9] Our experience with chlorpromazine coincided with that of some others,[10-16] in that the sedation was good in many cases, but was unpredictable in some instances and occasionally caused a precipitous fall in blood pressure. Needless to say, this has caused much apprehension on the part of labor room nurses, as well as ourselves.

We had previously used oral promethazine (an ethyl phenothiazine hydrochloride, which differs from chlorpromazine in having a branched side chain and in lacking the chlorine atom on the phenothiazine ring) for control of nausea and vomiting in pregnancy. A soporific effect was a frequent observation. Our clinical experience conformed closely to that reported in a study[17] conducted on normal subjects at an Army Air Force base, in which an electroencephalographic method was employed to evaluate objectively the sedative properties of various compounds. After a dose of 25 mg. of promethazine by mouth, the test subjects fell asleep in an average period of 26 minutes and 40 seconds. Our attention, therefore, was turned to parenteral use of promethazine* in the hope of developing a more satisfactory regimen for management of labor.

Plan of Study

This investigation was begun in May, 1955, and is continuing. Up to the time of this report (January, 1957), the series totaled 500 private patients ranging in age from 16 to 42 years, with an average of 27 years. About 50 per cent were primiparas. Gravidity ranged from i to xiii, and parity from 0 to xi.

All of these patients, even the most stable, exhibited some degree of nervousness and apprehension on admission, despite the careful prenatal instruction they had received. The younger primiparas particularly were disturbed by the discomforts attending the first stage. At the onset of each contraction such patients, without medication, usually become tense and fearful in anticipation of the full impact of the pain, regardless of reassurances and instructions to "relax." One 21-year-old primipara in this series (Patient 121), who had been hospitalized in the seventh month for treatment of vomiting and hysteria, showed extreme emotional distress.

Technique.—When labor was definitely established and the patient had begun to complain of the severity of the contractions, promethazine was administered intramuscularly. Scopolamine and meperidine, in varying dosages, were injected together in a separate syringe. The first few patients received 50 mg. promethazine, 50 mg. meperidine, and 1/150 or 1/200 grain scopolamine in the initial dose. This was repeated in 2 to 5 hours if necessary, and occasionally a third dose was given 3 to 6 hours later. Some received 75 mg. promethazine, 50 mg. meperidine, and 1/150 or 1/100 grain scopolamine, which in a few cases was repeated, with or without scopolamine, in 3 to 6 hours. As we gained confidence in the method, we increased the dose of promethazine to 100 mg., and used 25 to 50 mg. meperidine, with or without 1/150 to 1/100 grain scopolamine.

The majority of the patients received the first dose of premedication when dilatation of the cervix had progressed to about 3 cm. Many primiparas, however, received the first dose on dilatation to 2 cm. The blood pressure of the patient and the fetal heart rate were determined frequently before and after medication. Blood pressure readings ranged from 100/70 to 220/120 before medication and from 100/70 to 160/100 after medication.

Seven patients showed evidences of toxicity. In these the premedication blood pressure was 160/100 or higher.

*Promethazine hydrochloride is available as Phenergan-hydrochloride injection from the Wyeth Laboratories.

Anesthesia During Delivery.—The majority (80 per cent) were delivered under trichloroethylene analgesia and pudendal block with 1 per cent hexylcaine or procaine hydrochloride solution. In 3 per cent the standard gas-oxygen-ether combination was used, and in 6 per cent trichloroethylene analgesia alone sufficed.[18-19] Pudendal block or local infiltration of the perineum was all that was required in 3 per cent; and low spinal anesthesia was administered in 8 per cent, the unusually difficult cases.[20]

No tests were performed for sensitivity to the local anesthetic agents as a routine measure—often there was not time. The strong antihistaminic potency of promethazine may have contributed in some degree to the absence of allergic reaction in the patients in whom local anesthetics were used.

Delivery.—In 75 per cent of all patients at term delivery was spontaneous; low forceps were used in 14 per cent. Breech extractions were performed in 4 per cent; and in 3 per cent, rotation with Kielland forceps was necessary. Mid-forceps with manual rotation were used in 0.6 per cent, and cesarean section was required, after failure of trial labor, in 0.4 per cent. There were 7 pairs of twins and 9 single infants were delivered by breech extraction.

Results

In 15 to 30 minutes after the first injection, a definite general relaxation was noticeable, regardless of the size of the dose. On administration of subsequent doses, the onset of analgesia and sedation was even more rapid and the duration usually longer. Some of the patients dozed and others fell into a light sleep, from which at times they awakened temporarily as contractions became more forceful. They could be aroused easily, answered questions intelligently, and cooperated in response to directions. There appeared to be no interference with the muscular activity of the uterus; nor was there any of the "limpness" observed by Caroll and Hudson[10] in their chlorpromazine-treated patients, which they suggested might have been responsible in part for the prolongation of the labor seen in their series.

The great majority (88 per cent) of the patients received adequate sedation with one dose consisting of 100 mg. promethazine, 50 mg. meperidine, and 1/150 or 1/100 grain scopolamine, administered on dilatation of the cervix to 2 to 4 cm. A second dose, usually of 50 mg. of promethazine and 50. mg. of meperidine, but without scopolamine in some cases, was required by 10 per cent, in 3 to 5 hours after the first dose. Two per cent of the patients required a third dose, averaging 50 mg. promethazine, 50 mg. of meperidine, and 1/200 grain of scopolamine about 6 hours after the second. Included in this group was a primipara (No. 93) in whom manual rotation and midforceps delivery were required. She received two additional doses at intervals of 6 hours and 30 minutes after the third dose, during a total labor of 25 hours and 50 minutes. Adequate analgesia and sedation were also provided by similar doses administered during a trial of labor which preceded one cesarean section in the series. We now routinely use promethazine 100 mg., meperidine, 50 mg. and scopolamine, 1/150 grain, administered 2 hours before operation, in all cases of elective cesarean section, with excellent results.

Throughout labor the fetal heart rate ranged from 120 to 144, with an average of 140. In no case was there a change of maternal blood pressure suggestive of cardiovascular disturbance. In the 4 patients with definite hypertension the blood pressure showed a desirable fall of about 20 to 30 mm. Hg, and in the one patient with a premedication blood pressure of 200/120, the level fell 60 mm.—to 140/120. At no time was there a precipitous drop in previously normal blood pressure, nor was there ever a reduction to subnormal levels. Many of the patients were on their feet within 12 hours after delivery, but in no case did orthostatic hypotension occur.

Labor in this series appeared definitely shortened. The average duration of labor was about 9 hours, with an over-all range, in uncomplicated cases, of 20 minutes to 10 hours and 43 minutes from the first dose to delivery.

In 87 per cent of the primiparas, labor was without complication. Of the deliveries in this group, 96 per cent occurred within 1½ to 7 hours after the first dose. The range of total labor for these patients was 3 hours and 15 minutes to 11 hours and 43 minutes. It is especially notable that in 50 per cent of the primiparas with uncomplicated cases (in which premedication was administered on dilatation of 2 to 3 cm.), delivery occurred in 1½ to five hours, or after a total labor of 3 to less than eight hours.

The nurses frequently expressed satisfaction with the condition of the patients in the labor room, and commented that use of the compound lessens the supervision required.

All but one of the infants breathed immediately and cried spontaneously. The one exception was an 8 1/2 pound baby, a footling breech, with sudden prolapse of the cord, who was delivered under gas-oxygen-ether with forceps to the aftercoming head. This was the only instance in the series in which resuscitation was performed. There were no fetal or neonatal deaths.

No maternal deaths occurred. Blood loss at delivery was about the same as for patients managed by routine methods. There was no vomiting, but one primipara, in whom labor was prolonged by uterine inertia to a total of 19 hours, experienced some nausea.

None of the patients required barbiturates or opiates. The dosage of narcotic agents was greatly reduced. The total amount administered averaged 50 mg. of meperidine and 1/150 grain of scopolamine; whereas, with methods previously used, we had found it necessary to administer as much as 150 to 200 mg. of meperidine within the initial 3 hour period, and three doses of 1/100, 1/510, and 1/200 grain of scopolamine in the first 2 hours. Additional injections of meperidine and scopolamine were frequently necessary as labor progressed.

The patients in this series were often awake and talking calmly during repair of the episiotomy, and it was not unusual to be told, "This was a lot easier than I expected." On emerging from the delivery room most of them could speak immediately to husband and family, which was very reassuring to them.

There was no postpartum excitement and no evidence of "hangover," as are frequently seen after heavy narcosis. All patients were completely relaxed and a few were pleasantly drowsy throughout the day following delivery.

No toxic reactions were encountered after the use of promethazine in any amount, and there was no complaint of pain at the site of injection, until the volume of promethazine injected was increased to 4 c.c. (100 mg.) per injection. More recently we have found that this can be eliminated by intravenous administration, with the use of a smaller amount of promethazine. A similar experience was obtained in another study, in which promethazine was administered intravenously, in comparable dosage, prior to delivery of premature infants. No respiratory depression or other adverse effects occurred.

Comment

We have found analgesia and sedation predictable with this method, and believe the measures described will stimulate an important change in the management of labor. The obstetrician, of course, will be obliged to devote a little more time to each patient during pregnancy, persuading her that delivery can be accomplished without narcosis yet without excessive pain, and that the physical benefits to the infant are incalculable.

The influence of the premedication on the duration of labor appears especially noteworthy since it has been generally considered that normal labor

averages about 17 hours in length.[22-26] Various authors have reported a range of from 7 to 8 or more hours in uncomplicated cases in multiparas and from 11¾ to about 15 hours in uncomplicated cases in primiparas. The average total duration for young primiparas in a recent series of 196 patients[19] was reported as 11 hours and 10 minutes, and for elderly primiparas (34 years or older) as a little over 13 hours. In the study described by Carroll and Hudson,[10] total labor averaged about 17 hours for primiparas and about 10¼ hours for multiparas, with predelivery medication consisting of chlorpromazine and meperidine. With the small doses of promethazine, in combination with meperidine, employed in their series, the average labor in primiparas totaled 12¾ hours, and about 9¼ hours in multiparas.

The results of this study and those of others[10-21] suggest that promethazine may exert relaxant effect on the cervix without altering uterine contractions, but we have not observed relaxation of the perineal musculature.

Summary

Promethazine was administered to 500 private patients in an attempt to provide more adequate sedation in labor, yet avoid respiratory embarrassment in the infant. Premedication was first administered on dilatation of the cervix to 2 to 3 cm. In most cases adequate sedation was obtained with one dose of 100 mg. promethazine, administered intramuscularly, with 50 mg. meperidine and 1/150 or 1/100 grain scopolamine injected in a separate syringe.

Labor in uncomplicated cases was definitely shortened. In 87 per cent of the primiparas, labor was without complication; in 96 per cent of these, delivery occurred in 1½ to 7 hours after the first injection, and 50 per cent were delivered in a total of 3 to less than 8 hours. There was no respiratory depression in the infants as a result of the medication and, after a 2 year follow-up by their pediatrician, no delayed or unrecognized effect has been noted.

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ROUTINE HYPNOSIS FOR OBSTETRICAL DELIVERY

An Evaluation of Hypnosuggestion in 200 Consecutive Cases

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A STUDY of hypnosis in obstetrics was made to determine its value and dependability, not for the occasional spectacular procedure, but as a routine method for alleviating the pain of labor and delivery. The use of this modality is over a hundred years old, an original report by Durand[1] being published in 1860. During the last two decades many obstetricians have been studying this field,[2-6] and a huge number of successful isolated, individual cases have been reported. The record shows only a few large series,[7-12] however, where hypnosis has been used as a routine or quasi-routine procedure, with variations of from 20 to 80 per cent successful results.

The ideal anesthetic and analgesic agent in obstetrics is still being sought. This must be one having no toxic effects on either mother or child; one which selectively eliminates the pain sensation; one which promotes a maximum of voluntary cooperation and yet allows the mother the total experiences of childbirth. Since no such agent has, as yet, been found, many women fear the hazards of drugs for the reduction or elimination of pain of labor. This fear, together with the idea of "natural childbirth," "childbirth without pain," "drugless childbirth," and "childbirth under hypnosis," has been further developed by the lay press, which has left the distinct impression that woman must eschew medication for the "protection of her child."

Read[13] and others[14] attempted to bridge this gap by the promulgation of the idea that there is no such thing as unbearable pain during labor. They taught that the major discomfort experienced during labor was a manifestation of fear and panic, which could be overcome by proper education and training. This procedure left much to be desired, however, and untoward results have been reported.[15] Moreover, reports on the use of hypnosis for analgesia during labor seemed to fulfill so many of the requirements for an ideal anesthetic so well that the question presented itself as to whether or not a most valuable routine agent was being neglected.

It is not the aim of this discussion either to delve into the methods of induction, maintenance, and deepening of the hypnotic state, or to discuss the esoteric philosophy of the phenomena of hypnosis. Much scientific study has been directed toward these aspects, which are discussed in detail in the excellent texts of Clark,[12] LeCron,[16] Dorcas,[17] and Heron.[18] Similarly, it is not the function of this discussion to describe one, two, or three cases of successful and painless delivery by the sole use of hypnosuggestion. A truly unbiased

attempt was made to eliminate any preconceived ideas, prejudices, or superstitions, and to assay the worth of hypnosis in routine obstetrics. The present discussion is limited solely to the value of hypnosis as an analgesic and anesthetic agent during labor in a consecutive series of cases. In order to round out the study, other factors, including the effect of hypnosis on the duration of labor, the amount of bleeding at delivery, as well as the amount of time expended by the obstetrician-hypnotist, were also evaluated. These evaluations were made, not only by the obstetrician himself but also by obstetrical nurses, other obstetricians, pediatricians, and anesthetists.*

Material

A series of 200 patients undergoing labor was studied. With the exception of 18 patients who were referred primarily for hypnoanalgesia, all were private patients of the author. The entire study extended over 2 years. Deliveries were done in five different hospitals. An attempt was made to make the series a consecutive one, but this was impossible, since it was found that from 10 to 15 per cent of the women studied could not be hypnotized, and because 7 cases had to be excluded because they required anesthesia for emergency cesarean section or for breech extraction. All patients were physically and obstetrically normal. As far as could be determined by observation over a period of several months, no psychotic, masochistic, or otherwise mentally abnormal women were noted.

At the onset, it became obvious that, without exception, every woman responded in a different fashion to hypnosuggestion, not only during induction, but more especially during the time of labor. Evaluation of results was made after delivery (after the patient was returned to her room), and was weighed with other independent observations made during the labor process. Final results were grouped as successful or unsuccessful and placed in one of the following five categories:

Successful.—

1. *Ideal.* Complete anesthesia was present either during the trance state or in the awakened state as the result of posthypnotic suggestion (7 per cent).

2. *Successful.* Anesthesia might or might not be present during the labor process, but a complete posthypnotic amnesia was developed, and no conscious memory of the events which transpired while under hypnosis are recalled. Control of the patient was maintained at all times without the use of any supplementary medication (15.5 per cent).

3. *Mostly successful.* Good anesthesia was produced by hypnosuggestion during the first stage of labor, or a good, but not complete, posthypnotic amnesia for pain was present. Included in this group are the cases in which respiratory anesthesia was employed during the second stage because of inadequate control (24 per cent).

Unsuccessful.—

4. *Somewhat successful.* Absolute control of the first stage could not be maintained; the hypnotic trance state was spontaneously broken and could not be readily re-established, or when established was not satisfactory. Narcotics in less than normal amounts were used with the hypnotic state for relief of pain; minimal degrees of posthypnotic amnesia were developed. Inhalation anesthesia was employed in all cases (22.5 per cent).

*Obstetrical reaction and behavior during labor as the result of hypnosis will be discussed in a later paper.

5. *Unsuccessful.* The hypnotic state could not be induced at the time of labor, even though it had been successfully accomplished before. Also included are cases in which the trance was spontaneously broken and could not be re-established. Similarly, cases in which average doses of analgesics and anesthetics had to be employed are included in this category as well as those in which no posthypnotic amnesia could be developed after the completion of labor (31 per cent).

Without inclusion of the multitudinous factors involved in hypnosuggestion during labor, and with the use only of the criteria of analgesia, amnesia, and anesthesia, the 200 cases studied can be briefly summarized in Table I.

TABLE I. PAIN ELIMINATION BY HYPNOSIS DURING PARTURITION

	SUCCESSFUL			UNSUCCESSFUL	
PARITY	1	2	3	4	5
Primiparas	5	14	19	27	23
Multiparas	9	17	29	18	39
Total	14	31	48	45	62
%	7	15.5	24	22.5	31
		46.5%		53.5%	

In evaluating the control of pain (Table I), it must be remembered that the degree of severity and tolerance varies from individual to individual. This is true also of hypnosis and hypnosuggestion for the control of this pain during the labor process. All variations of patient control were noted, and in many instances it was most difficult to classify the result obtained. In retrospect, however, it is felt that, not only statistically speaking, but also in examination and study of each individual case, the control of the patient required more than the mere fact that hypnosis, even with prelabor training, had been employed. The mental attitude of the patient, the patient-obstetrician rapport, and the confidence of the patient in the procedure as well as in the accoucheur, seemed to be as important factors as was the hypnosuggestion itself. The elimination of pain, however, is not the only aspect to be considered. Other phases similarly must also be evaluated.

It has been frequently stated, and still more often quoted, that the duration of labor has been materially shortened by the use of hypnosis.[2, 7, 8, 9] We have attempted to evaluate this in the 46.5 per cent of the cases (categories 1, 2, and 3) where that hypnosuggestion worked satisfactorily. Comparison was made with cases where results were unsatisfactory, as well as with the labor records of 180 cases taken routinely from the files of one of the hospitals. Since it is difficult or almost impossible to determine the onset of labor, the starting point was the time of the patient's admission to the hospital. Obviously this too is inaccurate, but it was felt that a greater degree of exactness could be achieved in this manner. The end point was considered as the time of delivery. No distinction was made as to the type of labor, the position or presentation of the fetus, or the use of instruments in delivery. The time, in hours, from admission to delivery is expressed in Table II.

It has often been stated, and more often reiterated, that mental and physical relaxation is accompanied by a relaxation of the cervix, and consequently by a shortening of the first stage of labor. There is no question but that, with successful hypnoanalgesia and hypnosuggestion, a marked degree of relaxation is obtained. One should expect, therefore, a reduction in the length of parturition under hypnosis. This study (Table II) does not seem to bear this out, however. Although it is noted that the duration of labor in the hospital

with successful hypnoanalgesia was less in both primiparas and multiparas, the difference was not significant, and in this series cannot be considered to demonstrate a trend or tendency. On the other hand, where hypnosuggestion failed in the control of the discomfort of labor, the time of labor, on the average was increased, not only over the hospital average, but also over cases in which hypnosis was successful.

TABLE II. DURATION OF LABOR WITH AND WITHOUT HYPNOSIS

PARITY	NO. OF CASES	LENGTH OF LABOR IN HOSPITAL (HOURS)
Successful Hypnosis.—		
Primiparas	38	6.95
Multiparas	55	4.15
Unsuccessful Hypnosis.—		
Primiparas	50	8.05
Multiparas	57	4.25
Hospital Average.—		
Primiparas	80	7.48
Multiparas	120	4.27

Statements have also been frequently made that bleeding, both from the uterus and from the episiotomy, as well as during the postpartum period, was reduced with hypnonarcosis. This probably stems from the observation that a hypnotized person, when stuck with a needle, shows a minimum of capillary bleeding. Posthypnotic suggestions were given to all patients that minimal bleeding only would occur during the entire puerperium. We have attempted to assay this phase of hypnosis. Facilities for accurate weighing and measuring of blood loss, however, were not available. The total amount of bleeding in the delivery room was estimated by many independent observers and observation. It was generally agreed that, when hypnoanesthesia was employed to the exclusion of all other anesthetics, the blood loss was similar to, but no less than, when no anesthesia or sedation was used. Similarly, when cyclopropane, which seems to increase the amount of active bleeding, was combined with hypnoanesthesia, the blood loss was comparable to what occurred with cyclopropane combined with drug analgesics. In general, it was agreed by all observers that hypnosis, per se, had little or no effect upon the blood loss during delivery. Postpartum bleeding, both during the hospital stay (as measured by the number of perineal pads used) and also as to the duration in weeks after delivery, was compared in the several groups. No difference was noted. We cannot, therefore, assume in any way any diminution of the blood loss during the parturition process or during the postpartum period which could be attributed to hypnosuggestion.

Further study of the routine use of hypnosis in labor necessitated the consideration of the amount of time consumed in preparation of the woman before labor, as well as the amount of time necessarily spent with the patient in conducting the labor itself. At the beginning of this study, no specific program of indoctrination was followed, and attempts were made to induce a satisfactory trance state at the time of admission to the hospital. This proved to be unsatisfactory, however, because too many extraneous factors were present to allow for the necessary degree of subject concentration. Therefore prelabor training sessions were instituted. Forel[19] stated that, by repeating hypnotic suggestions at intervals, one or more phases of hypnotic control can be accentuated. He also stated that too many or too frequent sessions have a tendency to weaken the deeper effects of hypnosis. During the training sessions special emphasis was placed upon the ease of induction, the

projection and control of the labor process, the development of abdominal anesthesia, and the development of posthypnotic amnesia. The number of such preliminary exercises varied from none to seven or more, some being started as early as the fourth month, with the majority starting during the seventh month of gestation. A total of 593 such training periods were held for the 200 patients studied, most of which were individual. The results of preliminary training on the successful completion of hypnotically controlled labor is outlined in Table III. The time for each session varied between 25 and 50 minutes with an average of 30 minutes.

TABLE III. NUMBER OF PRELABOR INDUCTIONS AND SUCCESS OF HYPNOSIS IN LABOR

NO. OF TRAINING SESSIONS	NO. OF CASES	SUCCESSFUL		UNSUCCESSFUL	
		NUMBER	%	NUMBER	%
0	25	5	20	20	80
1	33	10	30.3	23	69.6
2	26	15	57.7	11	42.3
3	36	20	55.0	16	45.0
4	35	16	45.7	19	54.3
5	22	12	54.5	10	45.5
6	15	9	60.0	6	40.0
7 and more	8	6	75.0	2	25.0
	200	93	46.5	107	54.5

As can be seen, hypnosis in obstetrics, as a routine procedure or even for the occasional case, involves a tremendous amount of additional time when compared with obstetrical delivery with chemical narcosis. For routine use, this time element becomes maximally important. A study of Table III, therefore, throws a considerable amount of light upon this factor. It can be easily seen that the majority of best results occurred with the women who had two or more training sessions before labor, and that the degree of successful hypnosis increased with the amount of such preliminary training. Since the average time of each session was approximately 30 minutes, the total amount of training time approached two hours (593 sessions for 155 patients) for the individual woman. Also it is to be noted that the number of preliminary instruction periods did not help in cases where failure occurred.

This amount of time spent by the obstetrician-hypnotist is further increased by the time spent at the bedside during the labor itself. With the use of sedative and analgesic drugs, the parturient woman can be left with minimal supervision, and the obstetrician called only when delivery is imminent. This was not found to be true with hypnoanalgesia. The use of hypnosis, at least in our hands, demanded constant supervision, observation, and fortification. Attempts were made to transfer the rapport to understanding nurses or residents, but in general this was not satisfactory. To the time spent in training each patient must be added, therefore, the amount of time spent during labor. This means, then, that the obstetrician must be willing and able to devote 7 to 9 hours of individual attention to each patient who is to be delivered with hypnosis. For an obstetrician who delivers a hundred or more patients per year this becomes a physical impossibility. On this basis alone, the routine use of hypnosis becomes impractical.

It was also noted that the degree of the hypnoidal trance varied from patient to patient. This posed the question as to whether the depth of the hypnoidal state had a relationship to the analgesic results obtained with hypnosis during parturition. As is well known, the degree or stage of the trance

is a continuum, and as many as 11 different stages have been described, depending upon the response of the subject. For the purpose of this discussion, however, the depth of trance was classified in 4 categories (on the basis of the final session before parturition) as outlined by Heron.[18] Stage 1 was considered the lightest and Stage 4 the deepest. In Table IV the depth of the hypnotic trance is evaluated against the success of the hypnoanesthesia in 175 cases, the cases in which hypnosis was first employed at the time of the onset of labor being eliminated.

TABLE IV. DEPTH OF HYPNOSIS AND DEGREE OF SUCCESS, 175 CASES

DEPTH OF HYPNOTIC TRANCE	NO. CASES	SUCCESSFUL		UNSUCCESSFUL	
		NO.	%	NO.	%
1	27	8	29.6	19	70.4
2	36	20	55.5	16	44.5
3	76	37	48.7	39	51.3
4	36	23	64.0	13	36.0

Thus, from Table IV it can be seen that there is very little coordination between the depth of the hypnoidal state and the degree of hypnoanesthesia during labor. Some women, hypnotized only in the lightest degree managed their delivery successfully, while others, deep in the somnambulistic state were unable to cope with the discomfort of labor. Actually, so little coordination is present that it is impossible to predict in advance the outcome of the anesthetic effect during the labor itself, even though the women in the deeper states in general are more successful.

Comment

This study was made to determine whether hypnosis and hypnosuggestion could be used as a routine method for the control of pain during obstetrical delivery, similar to the routine methods with drugs and inhalation anesthesia. Purposely omitted here and left for future discussion are the methods of hypnotic induction, fortification, and development of posthypnotic suggestion. We have attempted to assay the hypnotic anesthetic effect in 200 consecutive private cases, eliminating only those in which obstetrical complications contraindicated its use, and to present, fairly and without prejudice or bias, all our observations.

It is well understood that the ideal anesthetic agent for the control of labor discomfort has not yet been found. The term "ideal anesthetic" must be defined. Primarily it must be safe and free from all possible harm for the laboring mother and her child. It must be one which gives complete control of pain, maintains and enhances patient cooperation, and allows the mother the psychological experience of the entire labor and delivery. It must maintain, and not destroy, the rapport between mother and baby which is set up at the time of the separation of the two as distinct individuals. It must insure the fact that the delivery experience carries with it most of the pleasant and few of the noxious features of parturition. Whatever agency or modality is to be employed must be easy to use, require a minimum of observation and instruction, and be predictably successful in all cases.

It is well understood that the same drug may act in dissimilar ways in different patients. All obstetricians have had the experience of giving large doses of narcotic and amnesic drugs without the slightest effect in controlling the pain of active labor. Similar results have been noted with hypnoanesthesia, and in certain cases hypnosis may be the most valuable agent for the control of pain and the management of labor.

In discussing the effects of hypnosuggestion on labor we must remember that this modality may be employed in a number of ways. Ideally it can be used as a means for producing anesthesia either in the trance state or as the result of posthypnotic suggestion. In this way the entire labor process may be remembered as a pleasant, vibrant experience without discomfort. In our study only 7 per cent of the total number of patients were delivered in this fashion. A second way which can be classified as satisfactory, but to a lesser extent, is by means of posthypnotic suggestions of complete amnesia for the entire experience. In 15.5 per cent this was accomplished with complete control of the patient's activity during the labor and delivery, the hypnotic suggestions of anesthesia and immobility also being used. In some of these cases evidence of pain being felt by the patient was noted during contractions and during the actual delivery, but recognition and memory of this pain were lost after the trance state was broken. An additional 24 per cent of the cases were classified as satisfactory even though it was necessary to employ inhalation anesthesia at the end of the second stage. This use of anesthesia was mandatory because good physical control of the patient during the delivery could not be maintained by the hypnosuggestions. No other medication was employed, however, and the result, from the point of view of the patient, as well as from that of the various observers, was considered to be good.

Thus in a total of 93, or 46.5 per cent, of the cases routinely studied, parturition was completed satisfactorily with hypnosis as the major anesthetic modality. This percentage of favorable results is not at all comparable with the results obtained with drugs, which approaches 95 per cent success.

Hypnosuggestion was considered to have failed in the remaining 53.5 per cent of the labors in which it was attempted, since other modalities had to be employed as the major measure for the relief of pain. This shortcoming of hypnosis becomes more than semantic, since no way of predicting success or failure could be ascertained. Although hypnoanalgesia and hypnoanesthesia roughly parallel the depth of the trance state (Table III), it was noted that this factor alone was not a guarantee of a satisfactory result. Furthermore, prediction of the final effect during labor, as based on observations of patient acceptance, depth of trance, acceptance of suggestion, etc., as made during the training sessions, were no better than pure guesses. No single or combined factors could be ascertained which would give a clue as to the final effect. From our observations, however, we were impressed by the fact that, in individual cases, the will to succeed, the rapport at the time of labor, and the mental attitude of the patient toward pregnancy and delivery were as important as the hypnosuggestion or the degree of the hypnotic trance.

One might, with some justification, ask whether this criticism of the routine use of hypnosis is justified, by stating that if proper rapport could not be obtained and failure of the trance state did occur, the obstetrician could always resort to medication. This, however, did not prove to be a valid objection for several reasons. First, it was noted that, while hypnosis did not seem materially to shorten the hospital time of labor, failure to maintain the trance state throughout the labor resulted in a lengthening of the parturition process (Table II). Second, in almost all of the cases where failure occurred, it was noted that relief of pain by adequate drug substitution did not appear to be the same in anesthetic effect as when drugs alone were employed. This observation was independently noted by a number of observers. Third, an effect similar to that found by Rogers[15] concerning failures with the Read technique was noted in many of the cases where hypnosis failed and medication had to be employed. In these there developed during the postpartum period a moderate to severe depressed state which could not be relieved by rehypnosis. No explanation for these sequelae can be offered at this time.

Last, if hypnoanalgesia or hypnoanesthesia is to be accepted as a routine or semiroutine procedure for the control of the untoward aspects of labor, then prelabor training must also be accepted, and the amount of time spent in developing and maintaining the hypnotic effect has to be weighed against the value and sureness of the results. As can be seen in Table III, three to four prelabor sessions, varying from 25 to 30 minutes each, seemed to produce maximal control. Thus approximately 2 hours was spent with each patient before even the onset of labor. Added to this was the necessity of almost constant attendance of the obstetrician during the labor to fortify the hypnotic state. This amount of time averaged 5¾ hours. This makes a total of 7½ to 8½ hours of constant attendance upon and complete preoccupation with the patient. If one were to consider that less than one-half of the total number of patients were able to manage their labors with the aid of hypnosuggestion, it can be calculated that for each successful case a total of 15 to 20 hours must be expended. Compared to one or two doses of Demerol, scopolamine, Seconal, and other commonly used medications for the control of labor pains, hypnosis becomes a tremendously expensive and time-consuming procedure, without commensurate return.

Summary

1. Hypnosis, in a very small number (7 per cent) of 200 cases where it was used, acted as the almost ideal modality for the pain and discomfort of labor.

2. In almost half (46.5 per cent) of the series where its routine use was evaluated, its action appeared to be satisfactory in the maintenance of anesthesia during labor and delivery. In these cases, fear, pain, and apprehension were reduced, cooperation improved, and the active experience of childbirth maintained.

3. The effect of hypnosuggestion is unpredictable in advance, and is not completely related to the depth of the hypnotic trance.

4. In this series we have not found that hypnosis has any effect upon the shortening of labor or decreasing the amount of postpartum bleeding.

5. On the other hand, failure to develop or maintain the hypnotic trance seemed to increase the time and severity of labor and to produce various degrees of postpartum depression.

6. On the basis of the present study, hypnosis cannot be recommended as a routine procedure for all parturient women. The special prelabor training and the constant attendance upon the patient during labor involve more time than the average obstetrician or general practitioner can afford or is able to devote.

7. Until the shortcomings of the modality can be overcome, hypnosis cannot be recommended as a routine anesthetic procedure for the pain of labor, but must be reserved for the occasional responsive patient.

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RUPTURE OF THE UTERUS

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RUPTURE of the gravid uterus is still one of the most serious catastrophes in obstetrics. Despite modern therapy, the maternal mortality associated with this accident remains high.

During the past two decades, many excellent articles[1-6] have appeared which have tended to crystallize our knowledge and management of this problem. It had been alleged that rupture in the lower segment is associated with a higher mortality than one in the upper.[7-9] It is not generally recognized, however, that most lacerations of the lower segment, extending through the external os, may also involve the vaginal wall. If colporrhexis is not detected, maternal death from hemorrhage may ensue despite apparently adequate abdominal surgery.

The purposes of this study are: (1) to review the experience of rupture of the gravid uterus at both a municipal and a voluntary hospital; (2) to direct attention to the fact that lateral lower segment tears involving the cervix commonly extend into the vagina; (3) to demonstrate that incomplete rupture of the uterus involving only the serosa and the myometrium does occur and produces a characteristic clinical picture, and (4) to emphasize that the most common cause of rupture of the uterus today is the dehiscence of a cesarean section scar.

TABLE I. INCIDENCE OF RUPTURE OF THE UTERUS IN 131,229 DELIVERIES AT THE JEWISH HOSPITAL OF BROOKLYN AND THE KING'S COUNTY HOSPITAL

HOSPITAL	YEARS	NUMBER OF RUPTURES	NUMBER OF DELIVERIES	INCIDENCE
Jewish Hospital of Brooklyn	1933-1954	52	89,616	1:1,723
Kings County Hospital	1944-1954	35	41,613	1:1,189
Total		87	131,229	1:1,508

Material and Incidence

Eighty-seven cases (1933-1954) of rupture of the uterus constitute the material for this study (1944-1954), 52 from the Jewish Hospital of Brooklyn and 35 from the Kings County Hospital. As noted in Table I, the incidence in the over-all series is one in 1,508 deliveries. The incidence at the municipal hospital is slightly greater than that of the voluntary institution. The incidence

at both centers would have been higher if all cases of occult or silent ruptures of cesarean section scars had been known for the entire period surveyed. Unfortunately, prior to 1953 at the Jewish Hospital and prior to 1951 at the Kings County Hospital, such ruptures, when asymptomatic, although noted at the time of operation, were rarely recorded.

Rupture of the Apparently Normal Uterus

A. Prior to the Onset of Labor.—Four cases of rupture occurred in the first two trimesters of pregnancy, one at the site of a previous cornual resection,[10] another in the rudimentary horn of a bicornuate uterus, and the remaining 2 as a result of erosion of the myometrium by a chorioadenoma destruens.[11] Rupture in the cases of chorioadenoma destruens occurred 4 and 6½ weeks after evacuation of the mole.

Although spontaneous rupture of the apparently normal uterus before labor is rare, recently Felmus, Pedowitz, and Nassberg[12] reported 121 cases from the literature, including 3 cases reported here.

B. During Labor.—Twenty-one cases composed this group, with 6 maternal deaths, a mortality rate of 28.6 per cent. These patients are generally characterized by advanced age and parity. Thus, 8 were 35 or more years of age and 10 had been delivered of four or more children prior to rupture (Table II and III). There was one primipara.

TABLE II. PARITY OF PATIENTS IN 87 CASES OF RUPTURE OF THE UTERUS

TIME AND ETIOLOGY OF RUPTURE	NO.	PARITY			
		0	i AND ii	iii AND iv	v AND OVER
A. Prior to Labor.—					
Bicornuate uterus	1		1		
Post salpingectomy	1	1			
Chorioadenoma destruens	2	2			
Spontaneous	3			1	2
Cesarean section scar	29		23	3	3
Myomectomy	4	3	1		
B. During Labor.—					
Cesarean section scar	5		4	1	
Myomectomy	1		1		
Spontaneous	21	1	8	4	8
Traumatic	20	3	12	2	3
Total	87	10	50	11	16

TABLE III. AGE DISTRIBUTION IN 87 CASES OF RUPTURE OF THE UTERUS

TIME AND ETIOLOGY OF RUPTURE	NO.	AGE IN YEARS			
		15-24	25-29	30-34	35-44
A. Prior to Labor.—					
Bicornuate uterus	1			1	
Post salpingectomy	1		1		
Chorioadenoma destruens	2	1	1		
Spontaneous	3		1	1	1
Cesarean section scar	29	8	9	9	3
Myomectomy scar	4			3	1
B. During Labor.—					
Cesarean section scar	5		3	1	1
Myomectomy scar	1			1	
Spontaneous	21	1	1	11	8
Traumatic	20	2	4	8	6
Total	87	12	20	35	20

Unrecognized cephalopelvic disproportion ranked second to high parity in the predisposition to spontaneous rupture (Table IV). There was very little correlation between the size of the infant and the incidence of rupture since only one infant was oversized (4,000 or more grams) whereas 3 were premature and 3 others weighed less than 3,000 grams.

TABLE IV. FACTORS PREDISPOSING TO SPONTANEOUS RUPTURE OF THE UTERUS DURING LABOR

High parity (iv or more)	10
Contracted pelvis	5
Previous cervical laceration	3
Forceful labor	1
Large infant	1
Impacted shoulders	1
Total cases	21

C. Traumatic Rupture.—There were 20 cases of traumatic rupture, with 3 maternal deaths, a maternal death rate of 15 per cent. Three of the patients were primiparas and 3 were multiparas. The age is noted in Table III.

Version and breech extraction are reconfirmed in this series as the foremost cause of traumatic rupture of the uterus, for 60 per cent of the traumatic ruptures reported herein were associated with this procedure (Table V). Generally the version was performed with ease; and in only one case was note made of any difficulty encountered. Rupture occurred in 3 cases with infants that weighed under 2,500 grams.

TABLE V. ETIOLOGY OF TRAUMATIC RUPTURE IN 20 CASES

Version and breech extraction	12
Breech extraction	3
Difficult forceps	2
Intramuscular oxytocin	2
Attempted manual removal of placenta accreta	1
Total cases	20

Breech extraction through an incompletely dilated cervix resulted in rupture in 3 instances. In one, the fetus weighed only 1,260 grams. Thus, breech extraction plus version with breech extraction accounted for 75 per cent of the ruptures in this category.

The selection of midforceps to accomplish vaginal delivery in 2 patients with undiagnosed midpelvic contraction also resulted in rupture of the uterus.

D. Location of the Rupture in the Apparently Normal Uterus in Labor.—As noted in Table VI, the cervix was involved in 25 instances and in 23 the laceration extended into the vagina. This involved not only the vault, but also, in many instances, the lateral walls. Five of the transverse lacerations in the lower segment extended into the broad ligament. Laceration was limited to the fundus in 7 cases. In 5, the integrity of the uterus was not completely compromised. In 2 of these the laceration extended from the endometrium partially into the myometrium and, in 3, from the serosal surface down to, but not including, the endometrium. These are the only cases which should have been classified as incomplete ruptures of the uterus without including lower segment ruptures which do not communicate with the peritoneal cavity.

In the latter type, there is complete disruption of the uterine wall through its entire thickness, which may be associated with profuse extraperitoneal hemorrhage from the vessels of the lower uterine segment and the broad ligament.

The designation of lower segment extraperitoneal rupture as "incomplete," also tends to minimize the seriousness of the accident. There were 9 deaths in the 41 cases of spontaneous and traumatic rupture of the uterus during labor and in no instance did the laceration communicate with the peritoneal cavity. In 8 the rent extended from the endometrial cavity into the broad ligament. The remaining one was truly "incomplete," involving the endometrium and partially extending into the myometrium.

TABLE VI. LOCATION OF THE LACERATION IN 41 CASES OF SPONTANEOUS OR TRAUMATIC RUPTURE OF THE UTERUS DURING LABOR

LOCATION OF THE RUPTURE	NO. OF CASES	NO. OF DEATHS
Vertical through fundus	5*	0
Horizontal through fundus	2	0
Vertical through lower segment	1	0
Horizontal through lower segment	2†	1
Lower segment through broad ligament	5	0
Lower segment through base of bladder	1	0
Lateral through cervix, external os, broad ligament	2	1
Lateral through cervix, external os, broad ligament, vagina	23	7
Total	41	9

*Includes 3 cases of incomplete rupture involving the serosa and myometrium.
†Both cases of incomplete rupture involving the endometrium and the myometrium.

Rupture Following Cesarean Section or Myomectomy

The dehiscence of a cesarean section or myomectomy scar is the most common cause of rupture of the uterus today. There were 34 cases of rupture of cesarean section scars and 5 following myomectomy. These 39 comprise 44.8 per cent of the total number of ruptured uteri.

If, as stated previously, all cases of silent rupture of cesarean scars were known, this group would probably exceed 50 per cent of the total.

The incidence of disruption of cesarean scar as reported by different authors[13-15] varies from 1.5 per cent to 10 per cent. At the Jewish Hospital of Brooklyn 24 defective scars were found in 235 patients subjected to repeat cesarean section, an incidence of 10.2 per cent. At the Kings County Hospital, since 1951 there have been 169 repeat sections; 10 of these demonstrated silent ruptures, giving an incidence of 5.9 per cent. As noted in Table VII, 27 of the ruptures were complete and 7 incomplete. Eight of the 34 ruptured scars were located in the upper segment and 26 in the lower. Of the latter, the previous incision had been transverse in 15 and vertical in 11. Twenty-nine of these patients were not in labor, and 5 of the operations were performed shortly after the onset of uterine contractions. Even in the latter group, the defective scar probably antedated labor since the physical appearance was identical with that of occult ruptures discovered prior to the onset of labor.

TABLE VII. LOCATION OF THE INCISION IN RUPTURE OF CESAREAN SECTION SCAR

LOCATION OF INCISION	TYPE OF RUPTURE			MATERNAL MORTALITY	
	COMPLETE	INCOMPLETE*	TOTAL	NO.	%
Classical	7	1	8	1	12.5
Vertical lower segment	7	4	11	0	0.0
Transverse lower segment	13	2	15	0	0.0
Total	27	7	34	1	2.9

*Figures on incomplete rupture represent those occurring at the Jewish Hospital of Brooklyn. These data are not available from Kings County Hospital.

The role of labor as a cause of disruption of a cesarean section scar cannot be ascertained from this series since both institutions rarely allow vaginal delivery following a cesarean section.

Fig. 1.

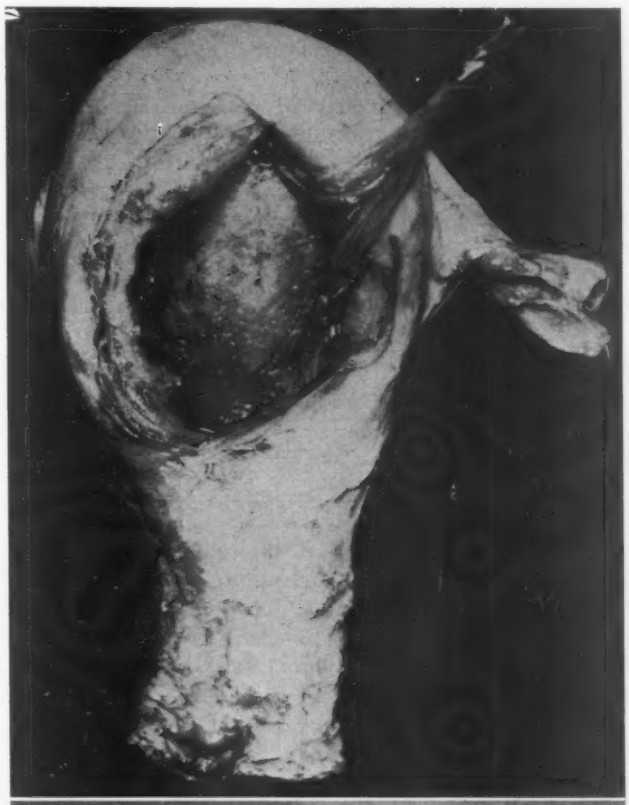

Fig. 2.

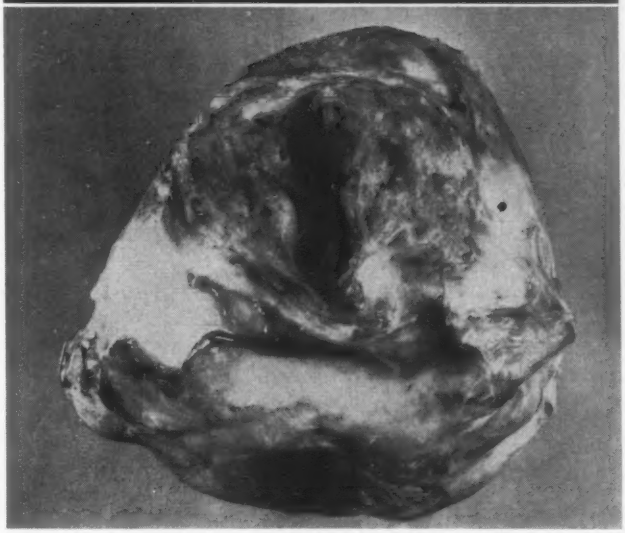

Fig. 1.—Uterus removed at autopsy, showing rupture of a classical cesarean section scar with placenta still in situ.

Fig. 2.—Uterus removed during elective cesarean section showing rupture of a previous myomectomy scar located in the posterior wall of the fundus. Note the exposure of the bed of the previously removed myoma. (Comparison with Fig. 1 demonstrates that a myomectomy may produce more extensive disruption of the myometrium than does a cesarean section.

Age seems to be of little significance. The majority of the ruptures occurred during the first or the second pregnancy following the initial section (Tables II and III). Multiple sections increased the tendency to rupture, however.

Although, Dewhurst and Rowley[16] as late as 1951 were able to collect only 66 cases of lower segment scar rupture from the literature, it is apparent from this study that rupture of a lower segment scar, whether transverse or vertical, occurs more commonly than has been realized. Lawrence[17] was unable to find any report of rupture of a transverse uterine scar without labor, yet all 15 cases reported here occurred prior to the onset of uterine contactions.

Table VIII illustrates that disruption of the scar can occur as early as the twenty-fourth week of gestation. All symptomatic ruptures occurred in classical scars (Fig. 1), however, 2 prior to the thirty-seventh week of gestation.

TABLE VIII. RUPTURE OF POSTCESAREAN OR MYOMECTOMY SCARS ACCORDING TO PERIOD OF GESTATION

INCISION	NO.	WEEK OF GESTATION				
		24	34	37	38	39
Cesarean section	34	1	1	4	18	10
Myomectomy	5	0	1	0	2	2
Total	39	1	2	4	20	12

Rupture of the uterus following previous myomectomy (Fig. 2) is one of the less common complications of pregnancy. Despite the fact that Pedowitz and Felmus[18] reported 35 such cases in 1952, Donald[19] in a recent text still feels that this rarely if ever occurs. Three of the 5 cases in this series are reported for the first time. The number of myomectomy scar ruptures reported in the literature now totals 47.[20-24]

Mechanism of Rupture of the Uterus

Most ruptures, when seen at the operating table, involve all three layers of the uterus. Incomplete tears, involving the endometrium and the myometrium, have also been described but incomplete rupture extending through the serosa and not completely penetrating the myometrium has rarely been reported.[25]

It is the general impression that rupture of the uterus originates from the internal surface and extends outward to involve the serosa. Thus, when 3 cases of incomplete rupture from the serosa into the myometrium occurred, they were regarded as curiosities, especially when histopathologic studies failed to disclose any lesion predisposing to rupture.

The gestational uterus is a hollow muscular organ and may be likened to a sphere. During labor, it attempts to expel the fetus through the cervical canal. The tension upon the individual muscle fibers of the contractile portion of the uterus varies inversely as the cube of its distance from the center. Thus, the fibers under the greatest tension are those located directly beneath the serosa and these are more apt to rupture early than those subjected to lesser tensions. It is therefore postulated that, in the apparently normal uterus where there is no endometrial or cervical defect, rupture is initiated from the serosal surface and extends into the depths of the myometrium. By the time the diagnosis is established the rent has extended through the endometrium in the vast majority of cases. The factor of increased tension is evident in the 3 instances of incomplete rupture of the serosa reported here. In one case, rupture occurred during a tetanic contraction induced by intramuscular Pituitrin. In

the remaining 2 cases, the laceration was initiated and extended during precipitate labor. Despite partial disruption of the uterine wall during the first stage, labor progressed and terminated in uneventful vaginal delivery.

Clinical Picture

The clinical picture depends upon the type of rupture and may vary from no symptoms at all to complete collapse (Table IX).

The absence of symptoms in 36 of the 84 cases of ruptured uteri may be attributed to the relative avascularity of scar tissue in 33 instances of rupture of cesarean section or myomectomy scars and the rapidity with which the diagnosis was made in 3 cases following version and breech extraction. It is the policy to perform routine intrauterine explorations following any intrauterine manipulation or difficult delivery. The absence of abdominal symptoms may also be attributed to the general anesthesia utilized for the version.

TABLE IX. SYMPTOMS IN 87 CASES OF RUPTURE OF THE UTERUS

TIME AND ETIOLOGY OF RUPTURE	SYMPTOMS						
	NONE	SHOCK	PAIN	ACUTE ABDOMINAL CRISIS	MASS	HEMATURIA	EXTERNAL BLEEDING
A. Prior to Labor.—							
Bicornuate uterus		1		1	1		
Post salpingectomy		1	1	1			1
Chorioadenoma destruens		2	2	2			2
Spontaneous		3	3	3			3
Cesarean section scar	26	2	3	2			
Myomectomy	3	1	1	1			
B. During Labor.—							
Cesarean section scar	3	1	2	2			1
Myomectomy	1						
Spontaneous		17	9	6	3	1	14
Traumatic	3	14	6	5	4		14
Total	33	42	27	23	8	1	35

The classical picture of uterine rupture was present in 51 cases, as noted in Table IX. Shock and external bleeding were observed in only one case of a ruptured uterine scar. Uterine contractions ceased following rupture in 7 of 23 cases in which rupture occurred prior to the termination of labor. In these cases there was also recession of the presenting part. In the remaining 16, despite evidence of uterine rupture, labor continued and vaginal delivery was accomplished either spontaneously or by means of low forceps. It is conjectured that the early signs and symptoms were due to incomplete uterine rupture and completion of the defect occurred as labor progressed and delivery was effected. This impression is strengthened by the fact that in 5 cases the laceration involved only 2 of the 3 layers of the uterus. It is further conjectured that, during labor, uterine contractions in the majority of cases cease only if the fetus is extruded into the peritoneal cavity. The state of contraction of the postpartum uterus is not indicative of the presence or absence of rupture. A relaxed postpartum uterus, supposedly characteristic of rupture, was observed in only 11 of the 34 patients in whom vaginal delivery was accomplished.

Incomplete tears extending from the serosa into the myometrium generally produce a characteristic syndrome. During labor, signs of uterine irritability

resembling that in abruptio placentae may be present. At delivery no abnormality of the placenta is found. Immediately post partum the possibility of rupture of the uterus is not suspected because of the paucity or absence of signs and symptoms. Exploration of the uterus is not informative for the defect does not involve the endometrial cavity. Any thinning detected is generally attributed to the usual variations in the thickness of the postpartum uterine wall. With the passage of time, shock becomes evident and increases in severity. This is accompanied by the development of peritoneal irritation and the finding of flank dullness. Laparotomy usually establishes the correct diagnosis. Occasionally rupture is asymptomatic and is accidently discovered during the performance of tubal ligation 24 or more hours post partum.

Treatment

The ideal treatment for rupture of the uterus is prevention of this catastrophe. Once rupture has occurred, immediate surgical intervention and adequate blood replacement are indicated. The surgical procedure employed must be individualized and is dependent upon the type, location, and extent of the perforation (Table X).

TABLE X. THERAPY IN 87 CASES OF RUPTURE OF THE UTERUS

Abdominal repair of uterine defect only	23
Abdominal repair of uterine defect and tubal ligation	4
Subtotal hysterectomy	29
Total hysterectomy only	5
Total hysterectomy with abdominal repair of vaginal laceration	12
Total hysterectomy with vaginal repair of vaginal laceration	5
Vaginal repair of laceration	1
Resection of bicornuate uterus	1
No surgery	7
Total	87

Separation of a previous uterine scar is best treated by excision of the old scar and repair of the defect. If there is an extension of the laceration into the adjacent myometrium, however, the election of repair is dependent upon the age, general condition, and parity of the patient, and the presence or absence of associated uterine pathology.

Prompt subtotal hysterectomy is indicated in rupture of the apparently normal uterus. If the cervix and vaginal wall are involved by the laceration, however, total hysterectomy is the treatment of choice.

In this series, there was an associated colporrhexis in 23 cases. In 12 of these, repair was done abdominally during the course of total hysterectomy, and in 5 others persistent profuse vaginal bleeding following hysterectomy led to exploration of the lower birth canal with discovery and repair of previously unrecognized vaginal lacerations. In 2 cases, despite establishment of abdominal hemostasis the patients' condition deteriorated rapidly and they died during the closure of the abdomen. Postmortem vaginal examination showed the source of the hemorrhage to be a previously unrecognized vaginal extension of the rupture.

In the remaining 4 cases, the hemorrhage was so massive that the patients died before operation could be performed. In 2 other cases, in which the laceration involved the cervix with no vaginal extension, total hysterectomy was performed in one case, with uneventful recovery; the other patient, treated by subtotal hysterectomy, died of unrecognized retroperitoneal hemorrhage.

Fetal and Maternal Prognosis

The over-all fetal and maternal mortality rates in this series are 33.3 per cent and 14.9 per cent, respectively. As is apparent from Table XI, the maternal and fetal risk are dependent upon the type of rupture. Since disruption of cesarean section scars accounts for more than 50 per cent of all uterine ruptures, it is obvious that the minimal fetal and maternal risk associated with this accident will tend to minimize the danger of rupture from other causes. It would, therefore, be preferable and more informative to express the mortality figures in relation to the type of rupture.

TABLE XI. FATAL AND MATERNAL MORTALITY IN 87 CASES OF RUPTURE OF THE UTERUS

TIME AND ETIOLOGY OF RUPTURE	NO. OF CASES	FETAL LOSS		MATERNAL MORTALITY	
		NO.	%	NO.	%
A. Prior to Labor.—					
Bicornuate uterus	1	1	100	0	0.0
Previous salpingectomy	1	1	100	0	0.0
Chorioadenoma destruens	2	2	100	0	0.0
Spontaneous	3	3	100	2	66.7
Myomectomy scar	4	0	0.0	0	0.0
Cesarean section scar	29	0	0.0	0	0.0
B. During Labor.—					
Myomectomy scar	1	1	100	1	100.0
Cesarean section scar	5	3	60.0	1	20.0
Spontaneous	21	12	57.1	6	28.6
Traumatic	20	6	30.0	3	15.0
Total	87	29	33.3	13	14.9

The fetal loss rate in the spontaneous ruptures was almost twice that in the traumatic. This may be explained by the fact that rupture in the traumatic group usually occurred during delivery or immediately thereafter, whereas in the spontaneous cases it usually occurred during the latter part of the first stage or early in the second. Labor continued and delivery was effected per vaginam in all. Six of the infants were lost while spontaneous completion of the second stage was being awaited.

Analysis of the maternal deaths shows that attempts at blood replacement without adequate hemostasis are of no avail. Accordingly, hemorrhage was responsible for 11 of the 13 maternal deaths reported herein. Seven of these resulted from profuse bleeding from unrecognized cervical or vaginal lacerations. Two other patients died despite massive transfusions, as a result of delayed diagnosis. Both patients had ruptures of apparently normal uteri prior to labor, and at that time it was not generally appreciated that rupture of the uterus could occur under these circumstances. Another patient with rupture of a classical cesarean section scar was admitted to the hospital in a moribund condition 14 hours after the onset of symptoms and she died shortly thereafter.

The eleventh maternal death occurred in a patient with postpartum hemorrhage in whom repeated attempts at uterine packing failed to control the bleeding. Administration of 2,500 c.c. of whole blood did not alter the outcome.

Postmortem examination showed an incomplete rupture involving endometrium and myometrium. This adds emphasis to the fact that some cases of postpartum hemorrhage are due to unrecognized rupture of the uterus.

The remaining 2 deaths were attributed to sepsis and to anesthesia; both occurred prior to 1940.

Comment

A laceration involving the lateral aspect of the lower uterine segment and cervix is far more serious than one in the fundus, and accounted for 7 of the 8 deaths due to rupture during labor. Subtotal hysterectomy is inadequate therapy in these cases, since it will not affect hemostasis when the cervix and vagina are involved. In this situation, total hysterectomy is indicated even though it is slightly more time consuming than the subtotal operation. It is accomplished more quickly and with greater ease in the pregnant than in the nonpregnant patient, however. Furthermore, once the cervical and uterine arteries involved have been ligated, a total hysterectomy is practically accomplished except for ligation of the parametrium on the uninvolved side. The additional few moments needed to complete the total hysterectomy will not materially increase the risk to the patient and will obviate the danger of continued hemorrhage from a laceration below the level of transection.

It is not generally appreciated that colporrhexis commonly occurs when the uterine laceration involves the cervix. When one realizes that the vaginal mucosa is reflected onto the cervix and that the parametrium is attached to the lateral aspect of the cervix and the vaginal vault, it then becomes obvious that complete laceration of the cervix will almost invariably involve the vagina. Because of the marked vascularity of this region, the resultant bleeding is often profuse and hysterectomy per se will fail to control the hemorrhage from the vaginal component of the uterine rupture. Thorough exploration of the vagina should be performed in all cases of uterine rupture involving the cervix, both prior to and following hysterectomy. If a laceration is discovered and visualization is not obscured by the hemorrhage, it should be repaired while the operating room is made ready.

Occasionally, the vaginal tear may be detected and repaired during the performance of the total hysterectomy. One most recent case illustrated these facts. Shortly after a spontaneous delivery, vaginal hemorrhage led to exploration of the birth canal with discovery and repair of a laceration of the sulcus. Because of the continued hemorrhage and progressively deepening shock, repeat examination showed the uterus to be ruptured. Total hysterectomy was performed with repair, abdominally, of an extensive laceration of the lateral wall of the vagina. During the procedure, the patient had received a total of 11,000 c.c. of whole blood. Because of vaginal bleeding following the completion of the hysterectomy, the vagina was re-explored. Two additional rents were shown to be the source of the brisk hemorrhage. During the repair of these tears, 2,000 c.c. of blood was transfused under pressure. Thereafter, the patient made an uneventful recovery.

Version, with its inherent dangers, is best relegated to history except for delivery of a second twin or the rare case of a multipara with a transverse presentation, who reaches full dilation with the membranes intact and in whom there is no evidence of cephalopelvic disproportion.

The relatively high incidence of rupture of previous cesarean section scars is a reflection of accurate recording of the condition of all scars at the time of elective cesarean section. The experience here is not unique, for similar results have recently been reported by others.[26]

Factors involved in rupture of uterine scars have been discussed in a separate paper.[27]

Summary and Conclusions

A review of 87 cases of rupture of the uterus showed a maternal mortality of 14.9 per cent and a fetal mortality of 33.3 per cent.

Incomplete rupture of the uterus involving the serosa and myometrium produces a characteristic clinical picture.

Colporrhexis commonly occurs when the uterine laceration involves the cervix. Failure to recognize and repair the vaginal laceration will result in death from continued hemorrhage.

Rupture involving the lower uterine segment is associated with a higher maternal mortality than rupture of the fundus.

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RUPTURE OF THE UTERUS: A TWENTY-YEAR REPORT FROM THE BOSTON LYING-IN HOSPITAL

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RUPTURE of the uterus constitutes one of the more serious complications of pregnancy. Although the over-all incidence has remained fairly constant in the last two decades, there has been a relative change in the number of ruptures attributed to a particular cause. Ruptures of the uterus due to obstetrical trauma have shown a marked decrease; this is the result of careful management, the use of clinical adjuncts such as x-ray pelvimetry, the elimination of hazardous obstetrical maneuvers, such as manual dilatation of the cervix or ill-advised internal podalic version, and the more frequent use of indicated abdominal hysterotomy. The resultant increase in the incidence of cesarean section, however, has brought about a relative increase in incomplete (silent dehiscence) uterine ruptures.

Sheldon[2] reported 26 ruptures, an incidence of 1:1,829, at the Boston Lying-in Hospital from 1918 through 1934. This report covers the period from 1935 through Oct. 31, 1955. Rupture of the uterus during this 20 year period occurred 84 times in 101,108 deliveries, an incidence of 1:1,204.

Spontaneous Rupture (Cesarean)

The uterine scar of a previous cesarean section remains the largest single predisposing factor to spontaneous rupture. This category of spontaneous rupture may be further divided into the *overt* and *silent* types. Our report includes 18 of the overt type and 42 of the silent type which together constitute 71 per cent of the total. Twenty-five cases in the latter group have been reported previously.[1]

Overt Rupture.—Overt rupture of the gravid uterus is usually associated with the well-recognized clinical picture of abdominal pain, hemorrhage, and shock, with or without vaginal bleeding. It may occur any time from the second trimester to term, associated or not associated with labor. The onset is usually sudden and without warning and consequently there is an associated high fetal and maternal mortality. In this group of 18 patients, there were 12 fetal deaths and 1 maternal death. The gestational age ranged from 26 to 43 weeks, with an average of 36.5 weeks. Table I summarizes the type of previous cesarean section, the presence or absence of labor, and the fetal and maternal mortality.

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In the 13 patients with corpus scars, there were 5 ruptures during labor. Two illustrative cases are as follows:

M. P., No. 19474, a 30-year-old gravida iii, para ii, entered the hospital at 38 weeks' gestation in mild labor. Her first pregnancy had been terminated by a classical-type cesarean section for a "deformed pelvis," with no test of labor. With her second pregnancy she had a precipitate delivery of a 6 pound infant. In view of her history and the clinical findings, it was decided to give the patient a test of labor. For 12 hours she had mild contractions with no progress. Suddenly the patient complained of severe suprapubic pain which spread to the lower abdomen and flanks. The fetal heartbeat was not audible. Laparotomy showed complete separation of the classical scar with a stillborn fetus and placenta lying free in the abdominal cavity. Subtotal hysterectomy was performed and an uneventful postoperative course followed.

G. F., No. 47297, a 28-year-old gravida iii, para ii, entered the hospital at 39 weeks' gestation in early labor. Her history disclosed a normal pelvic delivery followed 3 years later by a classical cesarean section for nontoxic premature separation of the placenta. During labor a sensitive, bulging mass was palpated beneath the abdominal scar. Laparotomy showed complete separation of the uterine scar with fetal membranes bulging into the peritoneal cavity. A vigorous 5 pound, 11 ounce infant was delivered and a subtotal hysterectomy performed. The postoperative course was uneventful.

These cases illustrate two important points: (1) classical (corpus) scars may rupture during labor, and (2) successful pelvic delivery following cesarean section does not preclude the possibility of rupture of the scar in subsequent labors.

Five cases of overt rupture occurred in patients with a history of lower segment cesarean section. Four of these patients were in labor prior to rupture. The following case history is representative.

B. F., No. 21097, was a 30-year-old gravida iii, para i. Her history disclosed a first trimester abortion followed by a lower segment cesarean section at term for toxemia, accompanied by vaginal bleeding. She entered the hospital at 43 weeks' gestation in labor, complaining of vaginal pain and a tearing sensation in the lower abdomen with each contraction. Immediate laparotomy disclosed complete separation of the lower segment transverse scar. A vigorous infant was extracted and a subtotal hysterectomy performed. The mother and infant did well.

The one patient not in labor presented a complicated clinical picture and a most interesting case:

M. L., RH No. 33025, a 23-year-old gravida ii, para i, with Class C diabetes (Priscilla White classification), had a lower segment cesarean section with her first pregnancy. At 32½ weeks' gestation she was hospitalized for abdominal pain, nausea, and diarrhea. Abdominal amniotomy was performed for acute hydramnios. One thousand cubic centimeters of fluid was withdrawn with the needle placed through the corpus. The initial fluid was clear but the last few hundred cubic centimeters were blood tinged. The element of infection was also present in the clinical picture, and a surgical consultant agreed to the possibility of acute appendicitis.

Laparotomy revealed a gangrenous appendix and 250 c.c. of grossly bloody peritoneal fluid. Palpation of the uterus showed a 7.5 cm. separation of the longitudinal lower segment scar. After appendectomy and closure of the right lower quadrant wound, a midline laparotomy and subtotal hysterectomy were performed. The patient did well but the infant succumbed in a few hours from prematurity and intrauterine asphyxia.

Another case illustrates the danger of generalization—in this instance, that lower segment scars are less likely to rupture than classical scars.

M. L., No. 21152, a 34-year-old gravida iv, para iii, had her first pregnancy terminated by "high forceps." She was delivered the second time by a lower segment (Kerr type) cesarean section, and the third time by a classical type hysterotomy. At 39 weeks' gestation in her fourth pregnancy she was awakened by sharp, steady upper abdominal pain. She was rushed to the Boston Lying-in Hospital and upon admission rupture of the uterus was apparent. Upon emergency laparotomy, a stillborn fetus and placenta, lying free in the peritoneal cavity, were extracted. There was complete separation of both the classical and lower segment scars. A subtotal hysterectomy and bilateral salpingo-oophorectomy were performed. The patient had an uneventful recovery.

Silent Rupture.—Silent rupture of the uterus is the term used for dehiscence of the previous uterine incision discovered at repeat cesarean section. Twenty-five of our cases were reported previously[1] and the subject discussed at length. Included in this report are an additional 17 cases encountered since Oct. 1, 1952. The type of uterine scar, and the fetal and maternal mortality are summarized in Table I.

TABLE I. SPONTANEOUS RUPTURE DUE TO PREVIOUS CESAREAN SECTION

		LABOR	NO LABOR
Overt.—			
Type of scar:			
Corpus	12	7	5
Lower segment	5	4	1
Corpus and lower segment	1	0	1
Total	18	11	7
Mortality:			
Fetal	12 (1 set of previable twins, 4 neonatal deaths including 1 from erythroblastosis)		
Maternal	1		
Silent.—			
Type of scar:			
Corpus	2	0	2
Lower segment	40	4 (3 had mild labor; 1 a 16 hour test of labor)	36
Total	42	4	38
Mortality:			
Fetal	4 (2 neonatal deaths, 1 from erythroblastosis, 1 from hemorrhagic disease of newborn)		
Maternal	0		

Spontaneous Rupture (Noncesarean)

Spontaneous rupture of the uterus occurred in 15 patients who had not undergone previous cesarean section. This group constitutes 18 per cent of the total number of ruptures. The vast majority occurred at term during labor; only 2 ruptures took place prior to labor. The maternal mortality was 3 (20 per cent) and fetal mortality 6 (40 per cent). Table II summarizes the cases.

TABLE II. SPONTANEOUS RUPTURE (NONCESAREAN)

Associated Etiological Factors.—		
Unknown	5	
Excessive size of fetus	2	
Dystocia due to brow presentation	1	
Pituitary extract	2	
Previously perforated uterus	1	
Cornual scar	1	
Cornual pregnancy	1	
Cervical scar	1	
Adenomyosis	1	
Total	15	
Labor.—		
In labor	13	
Prior to labor	2	
Total	15	
Mortality.—		
Maternal	3	
Fetal	6	(1 previable, 1 neonatal death at 36 hours)

Cause Unknown.—Five patients suffered spontaneous uterine rupture for no apparent cause. All of these were multiparas, one a gravida viii, para vi, and this may be a significant circumstance. One patient had an unprogressive labor associated with fetal distress, and the rupture was detected at cesarean section. Another patient had an uneventful labor with a low forceps delivery, and the rupture was discovered during exploration of the uterus for a retained placenta. One multipara had an uneventful labor with spontaneous delivery of a vertex presentation. She died of postpartum bleeding and shock, and the rupture was detected at postmortem examination. Another patient entered the hospital with the cervix fully dilated and had an outlet forceps delivery. She also died of postpartum hemorrhage and shock, and once again the rupture was found at postmortem examination.

Excessive Size of the Fetus.—In 2 cases the rupture was attributed to dystocia resulting from overly large infants. It is often difficult to assign excessive fetal size as the cause of rupture; in both instances, however, the infant weighed over 4,000 grams and no other factors were apparent with the possible exception of multiparity. An illustrative case follows:

A. B., No. 50018, was an unregistered 40-year-old gravida xii, para x, who was very obese. Labor began spontaneously at home and shortly thereafter her blood pressure was found to be 220/130. Five and one half hours after the onset of labor she was admitted to a community hospital and given magnesium sulfate. The blood pressure subsequently fell to 110/70, she experienced a tetanic contraction, the fetal heart tones became faint, and slight vaginal bleeding was noted. Labor became irregular and the patient lapsed into shock. She was admitted as an emergency to the Boston Lying-in Hospital and a diagnosis of ruptured uterus was made. The patient responded to emergency treatment and laparotomy revealed a transverse rupture of the lower uterine segment extending into the right broad ligament. A stillborn 11 pound, 5 ounce fetus with the placenta was lying free in the abdomen. A subtotal hysterectomy was performed. Approximately one hour postoperatively the patient again lapsed into shock with signs of intra-abdominal hemorrhage. The abdomen was re-explored and an attempt was made to ligate the hypogastric arteries, but the patient died on the operating table. Postmortem examination showed a recent patent tear of the right uterine artery near its source.

Dystocia Due to Brow Presentation.—One patient suffered rupture when she presented herself at term with a transverse lie which was converted to a vertex by external version. Labor was stimulated by a hot enema and castor oil and after 5½ hours a contraction ring was noted, associated with deflection of the vertex. At cesarean section the right lower uterine segment was found to be lacerated along with the cervix and right vaginal vault. The infant was stillborn, death being attributed to intrauterine asphyxia. A subtotal hysterectomy was performed and the mother had an uneventful postoperative course.

Pituitrin.—Two patients experienced rupture of the uterus after labor was electively induced by amniotomy followed by Pituitrin stimulation. One patient had had 4 normal pelvic deliveries. She was admitted from another hospital in shock and no fetal heart tones were audible. A subtotal hysterectomy was performed and the patient survived after a stormy postoperative course characterized by anuria from presumed acute tubular necrosis, ileus, and superficial thrombophlebitis of the lower extremities. The other patient, who had had 5 normal pelvic deliveries, had a tumultuous second stage with a precipitate delivery. The infant survived and the patient had an uneventful recovery following a subtotal hysterectomy.

Previously Perforated Uterus.—One patient suffered spontaneous rupture of the uterus at the thirty-fourth week of her second gestation. She had had a dilatation and curettage at another hospital after her first delivery for postpartum bleeding. Microscopically the curettings showed normal endometrial glands and fat. Although the pathologist considered the possibility of a uterine lipoma, the fat could well have been the result of perforation of the uterus at dilatation and curettage and have been a portion of omentum or mesentery brought down by the curette. The anterior fundus ruptured in the midline.

Cornual Scar.—Rupture occurred in one patient with a scar in the uterine cornu, the result of a resection for an ectopic pregnancy. Subsequently she had 5 pelvic deliveries including 3 breech presentations. Labor began spontaneously at 34 weeks and she was delivered normally. The placenta was retained for one hour and, after manual removal, a defect was palpated in the right cornu. An immediate hysterectomy was performed and recovery was without event. Microscopically the placenta had invaded the uterine scar and extended to the uterine serosa (placenta percreta).

Cornual Pregnancy.—One rupture occurred in a patient with a cornual pregnancy of 20½ weeks' duration. At laparotomy the rupture was found to extend from the right cornu to the midline of the fundus. This was evidently an incomplete rupture from without in. The interstitial pregnancy enlarged, thinning the adjacent myometrium and predisposing to rupture. It was necessary to perform a subtotal hysterectomy.

Cervical Scar.—There was one case of rupture of a scarred cervix and lower uterine segment, the result of a previous difficult pelvic delivery. This patient's second confinement was uneventful except for a final tumultuous labor. After a spontaneous delivery, exploration of the uterus revealed a 9 cm. defect of the right lower uterine segment and the cervix. An emergency laparotomy showed the anatomy of the right broad ligament and right retroperitoneal space to be grossly distorted by hemorrhage. A subtotal hysterectomy was performed and hemostasis was finally obtained by packing the right retroperitoneal cavity. The patient had a relatively uneventful recovery.

Adenomyosis.—A diagnosis of rupture of the uterus was made in one patient at term in labor with her first pregnancy. At laparotomy a left cornual defect was excised and the uterus preserved. Microscopically the excised specimen was a sinus tract containing adenomyosis.

Obstetrical Trauma

This report includes only 9 instances of uterine rupture as a direct result of obstetrical trauma. This group comprises 11 per cent of the total number of ruptures or one rupture in every 11,234 deliveries. The causes of rupture as well as the fetal and maternal mortality are summarized in Table III.

TABLE III. RUPTURE OF THE UTERUS DUE TO OBSTETRICAL TRAUMA

Cause.—	
Marked suprafundic pressure	3
Manual dilatation of cervix	2
Uterine trauma at cesarean section	2
Intrauterine manipulation	1
Unrecognized dystocia with stimulation of labor	1
Total	9
Mortality.—	
Fetal	3
Maternal	1

Excessive Suprafundic Pressure.—Three uterine ruptures were the direct result of excessive manual pressure applied to the fundus during delivery. In each instance the delivery note specifically mentioned that unusual manual force was applied to the abdomen. One obstetrician noted a "tearing sensation" beneath his hand as the pressure was being applied. We would like to emphasize the inherent danger of this obstetrical maneuver.

The three case histories are as follows:

M. F., RH No. 32480, a 30-year-old gravida iii, para ii, with a history of 2 normal pelvic deliveries, had an uncomplicated prenatal course and entered the hospital at term in labor. After an uneventful labor, a low forceps delivery was undertaken. After delivery of the head, shoulder dystocia was encountered which was treated with marked suprafundic pressure. Immediate manual intrauterine examination revealed a defect in the anterior lower segment. Emergency laparotomy confirmed the rupture and a subtotal hysterectomy was performed. Both the mother and infant did well.

J. W., RH No. 1010, a 34-year-old gravida iv, para iii, had a history of 3 normal pelvic deliveries. After an uncomplicated prenatal course she entered the hospital at term and had an unremarkable labor. Delivery was accomplished with low forceps accompanied by marked suprafundic pressure for delivery of the shoulders. Following delivery of the placenta the patient experienced hemorrhage and shock. Manual intrauterine examination disclosed a transverse rupture of the lower uterine segment extending laterally into both broad ligaments. Laparotomy confirmed the transverse rupture which had lacerated both uterine arteries. In spite of a subtotal hysterectomy, shock persisted and the patient died 12 hours after delivery.

B. B., a 27-year-old gravida ii, para i, had had one normal pelvic delivery and after an uncomplicated prenatal course entered the hospital at term in early labor. After an uneventful labor the vertex was delivered without the aid of forceps but shoulder dystocia was encountered. To aid the obstetrician marked suprafundic pressure was employed. Concomitant with the application of suprafundic pressure the obstetrician, who had one hand on the abdomen over the lower uterine segment, noted a "sensation of tearing." The placenta was manually removed and intrauterine examination revealed a longitudinal laceration of the lower uterine segment. Laparotomy confirmed the uterine laceration and a rapid subtotal hysterectomy was performed. Both the mother and infant did well.

Manual Dilatation of the Cervix.—There were 2 cases of rupture subsequent to manual dilatation of the cervix. Fortunately, this procedure has been abandoned and is no longer a factor in modern obstetrics.

Uterine Trauma at Cesarean Section.—In 2 cases the uterus was traumatized at cesarean section to a degree requiring hysterectomy. One rupture was due to a forceful removal of an unrecognized placenta accreta. The other occurred when, during extraction of the fetus through a corpus incision, an old lower segment scar was extended. Since the scar itself was thin, it was deemed best to perform a subtotal hysterectomy.

Intrauterine Manipulation.—Intrauterine trauma used to be a major cause of rupture. The present-day safety of cesarean section and other modern obstetrical adjuncts, however, have outdated difficult intrauterine manipulations. Only one rupture was incurred from this cause and this during a difficult breech extraction.

Unrecognized Dystocia.—One rupture occurred in a patient with an unrecognized 9 cm. obstructing leiomyoma located on the posterior uterine segment, associated with premature separation of the placenta. In accordance with the policy of that period, labor was stimulated by packing of the cervix and 1 minim of Pituitrin. The patient experienced severe abdominal pain and shortly thereafter rupture of the uterus was apparent. Immediate laparotomy confirmed the rupture and a dead fetus was found protruding through the uterine defect into the peritoneal cavity. A subtotal hysterectomy and right salpingo-oophorectomy were performed. The patient survived after a prolonged and difficult recovery complicated by a wound urinary fistula and pneumonitis.

Treatment

A successful outcome depends on a combination of rapid diagnosis and prompt, specific treatment. Whenever the diagnosis of ruptured uterus is suspected, the patient presents an acute obstetrical emergency. She should be prepared for immediate laparotomy and liberal quantities of whole blood should be available. A venous cutdown, and preferably two if time permits, should precede the laparotomy to insure a free flow of blood, as several transfusions will likely be needed. At laparotomy the most direct and expedient method of controlling the maternal hemorrhage should be employed. In most instances a rapid subtotal hysterectomy is the operation of choice. Unless the adnexa are involved, they need not be removed. Occasionally, especially in the instances of silent dehiscence, it is possible to denude the edges of the uterine wound and repair the defect. In instances of laceration into the broad ligaments with hematoma formation, where accurate identification of the uterine vessels is impossible, the surgeon should consider ligating the hypogastric branch of the common iliac artery on the involved side. The case reported (No. 50018) is a vivid example of the consequences incurred from insufficient uterine artery hemostasis, made difficult by an established huge broad ligament hematoma and retraction of torn vessels.

Postoperatively, the patients should be treated with adequate blood, fluid, and antibiotic therapy as indicated.

Comment

Our over-all maternal mortality was 5.9 per cent and the total fetal mortality was 29.4 per cent. These figures show a substantial decrease from those given in a previous report[2] from this clinic, and reflect the recent advances in the care of patients by avoidance of traumatic rupture and improved surgical care, with adequate quantities of blood to combat shock and antibiotics to control infection.

By far the largest single cause of rupture of the uterus during pregnancy is the scar of a previous cesarean section. Even in patients operated upon

with the best technical skill, with an afebrile postcesarean course, and subsequent careful prenatal care, rupture will occur in at least 3 per cent and perhaps more. There is no statistical evidence to prove that either corpus or lower segment sections have a greater degree of safety in regard to subsequent rupture. Some individuals have abandoned performing classical type hysterotomies, feeling that ruptures of lower segment scars bleed less and are "safer." Ruptures of lower segment scars, often extend into the broad ligaments, urinary bladder, or adjacent pelvic vessels, however, thus creating added hazards for the surgeon. Moreover, repeat cesarean section is no guarantee that rupture will not occur, as in many cases the uterine scars separate prior to the thirty-eighth week of gestation. Most obstetricians follow the old dictum, "Once a cesarean, always a cesarean," in an effort to prevent uterine rupture and other postcesarean difficulties. A point of interest is that during the period covered by this report 176 selected patients with a previous cesarean section were allowed to have one or more subsequent pelvic deliveries. Of these 176 patients only 2 (No. 47297 and No. 19474) (1.1 per cent) had ruptures of the uterus; there were no maternal deaths and one fetal death, an uncorrected fetal loss of 0.56 per cent. In this clinic it has been taught that rupture of the classical scar is more likely to occur during pregnancy when the myometrium is being stretched by the growing conceptus. By contrast, if rupture of the lower segment should occur, it would do so during the stress of labor. Further, it has also been taught in this clinic that, when patients with classical scars reach term, the latter had been sufficiently tested to make these patients safe candidates for pelvic delivery, provided obstetrical conditions were otherwise favorable. However, 38 per cent (5) of these patients suffered separation of the uterine scar during labor. These results tend to make us modify the view expressed above.

Spontaneous rupture of the uterus due to noncesarean causes constitutes the next largest group of cases. The causes are varied and this is probably the most difficult group in which to anticipate trouble. A history of a previous difficult pelvic delivery should alert the obstetrician. A careful intrauterine exploration and inspection of the cervix are mandatory in all such cases as well as those which require more than a low forceps nonrotation procedure. Multiparity and large infants are a continuing cause of spontaneous rupture. The unwarranted and injudicious use of Pitocin, especially in multiparas, is a contributing factor which can be avoided. Uterine inertia is a condition restricted in the main to primiparas. Should it occur in a multipara, other causes of dystocia should be excluded before labor is stimulated with Pituitrin.

Obstetrical trauma as a cause for uterine rupture has decreased through the years. In contrast to a previous series reported from this clinic where 65 per cent of the cases were directly attributable to trauma, in this series only 11 per cent were so caused. The inherent danger of suprafundic pressure is emphasized by the 3 cases here reported. The proved safety of outlet forceps in competent hands avoids the need of suprafundic pressure to assist the delivery of the vertex. When confronted with shoulder dystocia, the obstetrician should be able to reduce the impaction of the shoulders through the pelvis and any auxiliary force applied to the uterine fundus should be judicious and gentle. This is a difficult complication to treat. Our maneuvers for the treatment of shoulder dystocia are listed below in the order in which they are employed:

1. Gentle downward traction is exerted on the infant's head.

2. A finger is inserted into each axilla and gentle downward traction is exerted while the anterior shoulder is rotated into one of the oblique diameters.

3. The posterior shoulder is grasped, gently rotated, and delivered over the perineum, which allows the anterior shoulder to be delivered from behind the symphysis pubis.

4. The posterior shoulder is grasped and gently rotated through 180 degrees and delivered anteriorly (corkscrew effect). The now posterior shoulder is either delivered over the perineum or also rotated through 180 degrees and delivered anteriorly.

5. If the obstetrician is unable to rotate the shoulders, a hand is passed forward over the posterior shoulder and the chest wall until the infant's hand can be grasped. The arm is swiftly pulled over the infant's chest and downward, releasing the shoulder and facilitating delivery.

6. Cleidotomy rarely may be necessary. This procedure may be performed either under direct vision or by palpation. The clavicle should be divided in the midportion and care must be taken not to injure adjacent vessels and nerves. This is a rarely indicated and hazardous maneuver but is preferable to loss of the fetus or rupture of the uterus or both.

Barring cleidotomy, Titus's[3] comment bears repeating: "It is well to practice the maneuvers for shoulder delivery on normal-sized infants in order to become completely familiar with them before they become necessary."

Summary

1. During the 20 year period from 1935 through 1955, rupture of the uterus occurred 84 times in 101,108 deliveries, an incidence of 1:1,204. The over-all maternal mortality was 5.9 per cent and the total fetal mortality was 29.4 per cent.

2. The scar of a cesarean section was determined to be the cause of rupture in 60 cases (71 per cent). Eighteen of these were overt and 42 were silent (dehiscence).

3. Spontaneous uterine rupture occurred 15 times (18 per cent).

4. Obstetrical trauma was the cause of rupture in 9 cases (11 per cent).

5. The inherent dangers of suprafundic pressure are discussed and further emphasized by case histories of 3 ruptures caused by this obstetrical maneuver.

6. The dangers of pituitrin to stimulate labor, particularly in the multiparous patient, must continue to receive attention.

7. Methods of relieving shoulder dystocia including cleidotomy are enumerated.

8. It is difficult to take issue with the dictum "once a cesarean, always a cesarean."

9. It is concluded, therefore, that the most important single factor in preventing rupture of the uterus lies in *the indication* for the first cesarean section.

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RUPTURE OF THE GRAVID UTERUS*

Report of 40 Cases

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RUPTURE of the pregnant uterus remains a serious threat to the life of the mother and a greater hazard to the survival of the unborn infant. Eastman[6] said rupture of the uterus is responsible for 5 per cent of all maternal deaths. Beacham and Beacham[1] estimated that over 200 maternal deaths occur annually in the United States from rupture of the uterus. The maternal mortality rate in the United States has decreased in recent years. In 1954, 1,950 pregnant women died in this country. If, as is usually estimated, 5 per cent of these deaths resulted from rupture of the uterus, then 97 women lost their lives because of this complication of pregnancy.

The maternal mortality rate in Virginia in 1955 was 6.24 maternal deaths per 10,000 live births,[12] approximately one maternal death in 2,000 deliveries. Rupture of the pregnant uterus was reported as the known cause of 3.88 per cent of the maternal deaths in Virginia in 1955.[12] It is probable that rupture of the uterus caused twice as many deaths as were reported in the death certificates. In the past 5 years, 13 maternal deaths in Virginia are known to have resulted from rupture of the uterus. Therefore, at least 3.64 per cent of all the maternal deaths in Virginia during this 5 year period resulted from a complication which occurs only once in 1,600 to 2,600 deliveries.

We can reduce our present maternal mortality at least 50 per cent by education of patients as to the importance of early, regular, and consistent prenatal care, delivery and postpartum care; and the education of all physicians as to the prevention of certain dangerous complications, and the early recognition and proper treatment of some of the unusual, but unavoidable complications of pregnancy.

Incidence

The incidence of rupture of the uterus as reported in the literature is shown in Table I.

Rupture of the gravid uterus is an infrequent, but serious condition. Garnet,[7] at the Pennsylvania Hospital, in 1954, reported an incidence of one

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uterine rupture in 2,627 deliveries, with rupture occurring less frequently during the past 12 years. Beacham and Beacham,[1] in 1950, reported from the Charity Hospital in New Orleans a study of 96 uterine ruptures which occurred in 127,522 deliveries, an incidence of one rupture in 1,800 pregnancies. This report comprised not only a large group of cases, but it was a most complete analysis of the subject. Eastman[6] says the combined figures from four published series by Aken; Bill, Barney, and Melody; Delfs and Eastman; and Sheldon give a total of 117 ruptures of the uterus in 190,454 deliveries, that is, one in 1,627 deliveries. The incidence of rupture of the uterus following cesarean section, as reported frequently in the literature, is 1 per cent before the onset of labor and 1 per cent during labor.

TABLE I. REPORTED INCIDENCE OF RUPTURE OF THE UTERUS

HOSPITAL	PERIOD	AUTHORS	RUPTURES	DELIVERIES	RATIO
New York Lying-In	1909-1926	Davis	106	91.208	1:860
Philadelphia County	1931-1941	Dugger	105	318,103	1:3,029
Charity, New Orleans	1913-1950	Beacham and Beacham[1]	96	127,522	1:1,328
5 New York	1932-1946	Brierton	57	111,753	1:1,961
Johns Hopkins	1900-1945	Delfs and Eastman[6]	53	53,574	1:1,010
U. of Maryland and Baltimore City	1920-1943	Morrison and Douglas	45	65,916	1:1,465
Boston City	1920-1945	Lynch	44	41,706	1:1,118
Cook County	1928-1948	Fitzgerald, Webster, and Fields	42	92,226	1:2,196
Los Angeles County	1923-1934	McNeile and McBurney	30	17,350	1:578
Boston Lying-in	1918-1934	Sheldon[6]	26	47,554	1:1,829
		Bill, Barney, and Melody[6]	23	63,391	1:2,756
U. Hospitals of Cleveland and O.P.D. Western Reserve	1925-1941	Parker, J. C., and	22	35,253	1:1,602
Medical College of Virginia	1932-1949	Jones, G. R.			
Pennsylvania Hospital	1929-1952	J. D. Garnet[7]	21	51,186	1:2,627
Medical College of Virginia	1932-1956	Ware, Parker, Reda, and Jarrett	40	70,837	1:1,771

Approximately 60 per cent of our admissions are ward cases and 40 per cent private, with a total of over 6,000 deliveries last year. The hospitals admit many emergency cases, both from Richmond and from a distance of 100 miles or more.

During the past 25 years, as shown in Table II, we have had one rupture of the uterus in every 1,771 deliveries at the Medical College of Virginia Hospitals. Many of the ruptures occurred before the patients were admitted to the hospitals.

TABLE II. INCIDENCE OF RUPTURE OF THE UTERUS AT THE MEDICAL COLLEGE OF VIRGINIA HOSPITALS

	NO. OF CASES	NO. OF DELIVERIES	RATIO
1932 through 1949	22	35,253	1:1,602
1950 through 1956	18	35,584	1:1,976
Total	40	70,837	1:1,771

Classification

Several different classifications of rupture of the uterus appear in the literature. One of the simplest is: (1) rupture of the previous cesarean scar, (2) spontaneous rupture of the intact uterus, and (3) traumatic rupture of the intact uterus.

We will use in this paper a more detailed classification as shown in Table III which we think helps to indicate the changing trends in obstetric care.

TABLE III. RUPTURE OF THE UTERUS AT THE MEDICAL COLLEGE OF VIRGINIA, 1932 THROUGH 1956

Before Labor.—	
1. Spontaneous rupture of	
a. Previous cesarean section scar	7
b. Previous operative scar	0
c. Intact uterus	2
2. Traumatic rupture	0
During Labor.—	
1. Spontaneous rupture of	
a. Previous cesarean section scar	9
b. Previous operative scar	0
c. Intact uterus	7
2. Traumatic rupture	15

Traumatic rupture occurred in 18 of our patients, and rupture of a cesarean scar was seen in 16 patients. Internal podalic version and breech extraction were the cause of 8 traumatic ruptures. Six patients who had ruptured uteri were delivered with forceps, and oxytocics were used in 3 cases. Three patients who were delivered at home with forceps were later admitted to the hospitals, and 2 who received oxytocics at home were hospitalized after the rupture occurred.

The decrease in the use of high forceps and internal podalic version and breech extraction, and the more frequent use of cesarean section for delivery in transverse presentations, placenta previa, and premature separation of the placenta have decreased the frequency of traumatic deliveries and the relative incidence of this type of rupture.

Our studies show that a preponderance of noncesarean uterine ruptures occurred in the older groups, as reported by others in several papers. Postcesarean ruptures occur more frequently in younger patients.

TABLE IV. RUPTURE OF THE UTERUS AFTER CESAREAN SECTION

Type of Section.—		
Corporal	14	
Lower segment	2	
	16	
Indication.—		
Generally contracted pelvis	5	
Funnel pelvis	1	
Cephalopelvic disproportion	3	
Pre-eclampsia	1	
Eclampsia	2	
Uterus didelphys	1	
Pyelitis	1	
Unknown	2	
	16	
Mortality.—		
Maternal	0	
Fetal	6	(37.5%)

Rupture of the pregnant uterus occurs most frequently at or near term. It occurred in 7 of our former cesarean patients before the onset of labor and in 9 former cesarean cases after the onset of labor (Table IV). We think it is difficult to predict with any degree of accuracy which cesarean section scar will rupture. We believe a scar in the fundus of the uterus may rupture more

frequently than one in the lower segment, and that a transverse cesarean section scar in the lower segment of the uterus is less likely to rupture than a longitudinal scar. Rupture of a scar in the cervix or lower segment carries a real danger of injury to the bladder, but if the rupture is in an old cesarean scar, it may not produce as severe hemorrhage as a rupture in the upper half of the uterus, unless the placenta is implanted abnormally low, and at the site of the rupture.

Symptoms and Signs

One must remember that analgesia and anesthesia will mask symptoms of rupture in some patients and may cause a dangerous delay in the recognition and treatment of this serious complication.

Tenderness of the uterus, particularly if an old scar is present, is an important symptom. Failure of labor to progress if uterine contractions are good, suggests the possibility of rupture of the uterus. Dr. Willard Cooke[3] has pointed out that the "intuition of the patient and pain of a diaphragmatic type may be associated with rupture of the uterus."

In cases of actual rupture of a spontaneous type (Table V), the patient characteristically experiences a tearing pain at the time of rupture, if she is awake. Abdominal pain usually increases just before the rupture occurs. If the baby is extruded from the uterine cavity into the peritoneal cavity, there will be recession of the presenting part. Fetal movements may be active just preceding or during the rupture, but soon disappear if the rupture is extensive or complete, and fetal heart sounds disappear quickly. Shock and hemorrhage occur frequently and may rapidly cause death unless the patient is operated upon immediately and transfused with whole blood when indicated. If the baby is expelled from the uterine cavity into the peritoneal cavity, the uterus usually contracts rapidly to the size of a 4 months' pregnancy, but hemorrhage may be profuse.

TABLE V. SPONTANEOUS NONCESAREAN RUPTURE OF UTERUS

Brow presentation	1		
Transverse lie	1		
Hydrocephalus	1		
Cephalopelvic disproportion	2		
Placenta accreta	1		
Penetrating hydatid mole	1		
Unknown	3		
		10	
Patients not in labor	2		
Patients in labor	8		
		10	
Maternal deaths:			
Septicemia and peritonitis	2		
Shock and hemorrhage	4		
		6	
Fetal deaths		9	(90%)

Black[2] has pointed out that "shock is not a constant feature of rupture of the uterus. Thus, one should not regard the presence of shock as an absolute criterion in making a diagnosis of rupture of the uterus."

Rupture of Cesarean Section Scar

The high incidence of rupture in the corpus of the uterus in our patients may be due to the fact that, prior to 1932, most cesarean sections in our section of the country were classical sections. In recent years, our cesarean sections

are practically all cervical sections and, consequently, the incidence of rupture in cervical sections has increased. The locations of the ruptures are shown in Table VI.

TABLE VI. LOCATION OF RUPTURE

	SPONTANEOUS	TRAUMATIC	CESAREAN
Corpus	1	0	13
Corpus and lower segment	2	3	0
Lower segment	6	12	3

Any discussion of rupture of the gravid uterus necessitates a consideration of the danger of rupture of a cesarean scar in a subsequent pregnancy and labor. Obstetricians are fairly well divided in their thought about this subject. Cosgrove[4] says in a recent paper, "I am taking my stand firmly with the school which believes that a woman who has had to have one cesarean will not necessarily be compelled to have a repeat section with any or all of her subsequent pregnancies." All of us who know Dr. Gosgrove have the deepest respect for his judgment and ability, and he is recognized as one of the outstanding obstetricians of our time.

In 1956, Dr. Cosgrove reported a total of 158,498 deliveries and 5,407 cesarean sections performed at the Margaret Hague Hospital. Thirty-three ruptures of the uterus through previous cesarean scars occurred in these cases. Only 6 of the ruptures occurred prior to labor and only one woman died from rupture of the uterus following previous cesarean section. Cosgrove reported that following 500 cesarean sections 179 women, 35.8 per cent, were delivered of 221 babies vaginally. These are convincing statistics, but few hospitals are as well organized and staffed as the Margaret Hague, and most of us cannot expect to equal the results of Dr. Cosgrove and his excellent staff.

Douglas[5] states that 35 per cent of the patients delivered by cesarean section at the New York Lying-In Hospital, Cornell Medical Center, are delivered vaginally in subsequent pregnancies. Schmitz and Baba,[11] in 1949, reported a study of 385 patients delivered by cesarean section; 157 of these subsequently became pregnant, and 51 (32.4 per cent) were successfully delivered vaginally. In 3 cases the uterus ruptured, but all 3 mothers survived. Schmitz and Baba concluded their paper with the statement: "The old dictum 'Once a cesarean section, always a cesarean section' should be changed to 'Once a cesarean section, not necessarily always a cesarean section.'"

Meredith[9] reported from the Woman's Hospital of New York 36 cases of rupture of the uterus in 32 years. Twenty-two, or 61 per cent of the ruptures occurred in women who had been previously delivered by cesarean section. His report included 13 silent or incomplete ruptures.

Johnston and Morgan,[8] at a recent meeting of the Southern Medical Association in Washington, reported a study of 2,402 cesarean sections and 641 repeat cesarean sections, an incidence of 26.7 per cent repeat sections during the period 1938 through 1955. These authors reported a fetal and infant loss of 1.16 per cent in vaginal deliveries, 5.50 per cent in primary cesarean sections, and 0.78 per cent in repeat sections. They reported 29 ruptures of the uterus, an incidence of one in 3,180 deliveries. Nineteen, or 65 per cent of the ruptures, occurred in patients previously delivered by section.

Meredith[9] reported 36 cases of ruptures of the uterus between 1921 and 1952. Twenty-two, or 61 per cent, of these patients had been previously delivered by cesarean section.

A patient who has had a delivery by cesarean section can later have a vaginal delivery under certain conditions. When a vaginal delivery is planned after a former cesarean section, the pelvis must be ample and there should be no question about cephalopelvic disproportion or an abnormal presentation or position of the fetus. The patient must be in a well-supervised and adequately staffed hospital. Her blood should be Rh and group typed, and blood which has been properly cross-matched should be held in the blood bank available for immediate use. The operating room should be available on short notice. Even patients with uneventful recoveries after cesarean section sometimes have weak scars. If the patient has a stormy convalescence after her cesarean section, she is a poor risk for a later vaginal delivery.

Any physician who elects to deliver vaginally a patient who has had a cesarean section should certainly stay with the patient while she is in labor, and be prepared to operate upon her immediately if she has signs or symptoms suggesting a rupture of the uterus. Any patient delivered vaginally after a previous cesarean section delivery should have an intrauterine examination after the placenta has been delivered, in an attempt to rule out rupture of the uterus. We think exploration of the uterus should be done after any difficult delivery, either with forceps or with internal podalic version and breech extraction, and after any delivery with excessive uterine bleeding.

Mortality

Table VII shows the maternal and fetal mortality associated with the different types of rupture of the uterus.

TABLE VII. MATERNAL AND FETAL MORTALITY

Traumatic Rupture.—		15 cases
Maternal deaths	4 (26.66%)	
Fetal deaths	12 (80.00%)	
Rupture Following Cesarean Section.—		16 cases
Maternal deaths	0 (0%)	
Fetal deaths	6 (37.5%)	
Spontaneous Rupture.—		9 cases
Maternal deaths	6 (66.66%)	
Fetal deaths	9 (100.0%)	

Since 1932, 40 patients with ruptured uteri have been treated in the Medical College of Virginia Hospitals, and 10 of these died, a mortality rate of 25 per cent (Table VIII). Four patients were not operated upon. Two of these entered the hospital 24 and 48 hours, respectively, after delivery in their homes, and died from hemorrhage and shock soon after admission. A third patient had several unsuccessful forceps attempts at home, entered the hospital moribund, and died undelivered soon after admission. The fourth patient died undelivered in the hospital, following sudden rupture of the uterus and massive internal hemorrhage after 7 hours of irregular and weak uterine contractions. A fifth patient died of a penetrating, nonmalignant mole 6 months following a spontaneous abortion. The sixth patient died from rupture of the uterus, hemorrhage, and shock, near term, 14 months after a previous difficult vaginal delivery.

Another death resulted from a transverse presentation, with prolaped left shoulder and arm. The eighth death resulted from a version and extraction after previous attempts at delivery at home had failed. Another patient died from hemorrhage and shock resulting from a ruptured uterus because of cephalopelvic disproportion. The tenth death resulted from septicemia following rupture of the uterus.

Table VIII also shows the decrease in mortality during the past 7 years.

TABLE VIII. RUPTURE OF THE UTERUS AT THE MEDICAL COLLEGE OF VIRGINIA HOSPITALS FROM 1932 TO 1950 (25 YEARS)

YEARS	NO. OF CASES	MATERNAL DEATHS		FETAL DEATHS	
		NO.	%	NO.	%
1932-1949	22	8	36.36		
1950-1956	18	2	11.11		
1932-1956	40	10	25.00	27	60.75

Summary

Rupture of the uterus is a dangerous complication of pregnancy which often results in death of the mother and fetus.

Rupture of a cesarean section scar is the most common type of rupture in recent years. It probably occurs as frequently following cesarean section of the cervical type as it does following the old classical type section.

The first cesarean section should be done only for very definite indications, and in many patients with borderline pelves a few hours (6 to 8) of trial labor will sometimes make the contemplated cesarean section unnecessary.

Careful selection of patients with real indications for the first cesarean section will decrease to a minimum the argument about vaginal delivery after cesarean delivery.

We attempt vaginal delivery after cesarean section in only a limited group of selected patients.

Rupture of the uterus is decreasing in frequency. The maternal mortality associated with this complication has probably been decreased by the use of antibiotics and transfusions with whole blood.

During the past 7 years, eighteen patients with ruptured uteri have been treated in the Medical College of Virginia Hospitals. Two of these patients died, a maternal mortality of 11 per cent.

Better prenatal care and the avoidance of traumatic deliveries will enable us to reduce the maternal and fetal mortality resulting from rupture of the uterus.

We wish to thank Drs. Joseph C. Parker and George R. Jones[10] for the use of their material in the early years of this study.

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RUPTURE OF THE UTERUS DUE TO PLACENTA ACCRETA AT THE SITE OF A PREVIOUS CORNUAL RESECTION

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TWO unusual causes of spontaneous rupture of the pregnant uterus are a previous cornual resection and placenta accreta. Only 4 cases of the former could be found in the past 30 years, and only one of these occurred at term.[1-4] About 15 cases of placenta accreta causing rupture of the uterus have been reported.[5] We wish to present a case of a spontaneous rupture of a pregnant, full-term uterus due to placenta accreta at the site of a previous cornual resection. Although this is a likely combination, we have been unable to find a similar case report elsewhere.

E. B., a 26-year-old woman, para i, was admitted to Harlem Hospital on May 9, 1957, after being transferred from another institution. She had been delivered by low forceps of a live full-term infant on May 6, 1957. The labor and delivery had proceeded normally, and the placenta had been spontaneously delivered, but was noted to be rather small. Blood loss was minimal. About one and one-half hours after delivery, the patient suddenly went into profound shock. The blood pressure and pulse were unobtainable. There was no external bleeding or signs of intra-abdominal hemorrhage, nor were there any signs or symptoms of pulmonary embolism. A manual exploration of the uterus was done but a rupture could not be felt. The possibility of an allergic reaction to meperidine was considered. The patient was given 1,000 c.c. of blood and an infusion containing Levophed, and the blood pressure returned to normal.

The next day the patient had slight abdominal distention, and the following day the distention seemed to be increasing slightly. A blood count showed 1.9 million red cells and a 40 per cent hemoglobin. The blood pressure was 120/80, pulse 120. She was given another 500 c.c. of blood but late that evening she again went into shock. Another transfusion was started and she was transferred to Harlem Hospital.

The past history of the patient was negative for any systemic diseases, including sickle-cell anemia. On July 3, 1956, she had been operated on at Harlem Hospital for a ruptured ectopic pregnancy, at which time a left salpingo-oophorectomy with cornual resection had been done. Her postoperative course had been uneventful. She did not menstruate after that date and had apparently become pregnant at the first ovulation following the operation.

At the time of the present admission, she presented the following findings: pulse was 120, blood pressure 90/40, respirations 28 per minute, and the temperature was 100.6° F. The conjunctivae were very pale. The abdomen was distended, tense, and tender. Shifting dullness and a fluid wave were elicited. Pelvic examination was unsatisfactory because of the distention and tenderness. The hemoglobin was 40 per cent.

A laparotomy was done shortly after admission. The abdominal cavity contained about 3,000 c.c. of blood. The uterus was the size of a 12 to 14 weeks' pregnancy. The left tube and ovary were absent. A 6 cm. hemorrhagic mass bulged out from the region of the left cornu. Large blood vessels coursed over this area. The remainder of the uterus and the right tube and ovary appeared normal. A total hysterectomy was performed. The patient's postoperative course was uneventful except for some abdominal distention for the first 3 days. She was given several more transfusions and was discharged on the eleventh postoperative day.

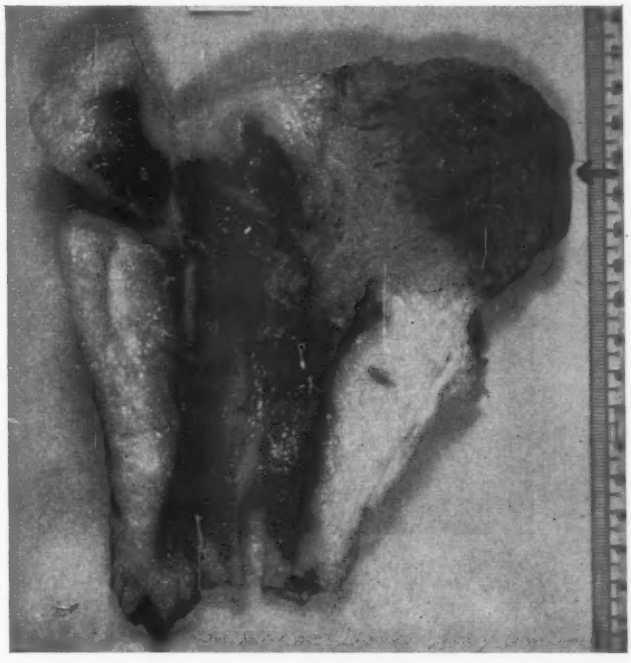

Fig. 1.—The uterus opened to show the placental tissue implanted in the left cornu and the thinned-out myometrium. The point of rupture is indicated by the arrow.

Gross description of the specimen was as follows: The uterus measured 15 by 11 by 6 cm. A mass bulged out from the left cornu and there was a defect in the uterine wall here. Soft, spongy, purple tissue protruded through this defect. When the uterus was opened, it was seen that the region of the left cornu had been dilated by a mass of placental tissue, about 6 cm. in diameter. There was no plane of cleavage between the mass and the uterine wall. The myometrium was 3 cm. thick, except at the left cornu where it gradually thinned out, until at one point it had finally been split open (Fig. 1).

Microscopically, the myometrium at the left cornu was very thin and had been partly replaced by scar tissue. Placental tissue lay in and on the scar tissue and there was little decidual reaction in this area. Sections through other parts of the uterus showed a normal decidual reaction. The pathologic diagnosis was "herniation of adherent retained placenta through split myometrium of the left cornu."

Comment

At Harlem Hospital, a deep cornual resection is usually done whenever a tube is excised. Such a procedure had been carried out on this patient. Within a few weeks following this, she conceived, and part of the placenta was implanted at the site of the resection. Even normally, the uterine cornu is an area of endometrial deficiency. Also, a placenta implanted in a cornu has a thin, atonic underlying myometrium and may not separate spontaneously.[6]

In this case, with the additional trauma of recent surgery, ideal conditions for a placenta accreta were present. One can only speculate on the immediate cause of the rupture. Was it due to the placenta accreta or would it have occurred even if part of the placenta had not been implanted there? We believe that the placenta had much to do with further weakening the already thin and damaged uterine wall.

This leads to a discussion of the merit of doing an extensive cornual resection with salpingectomy. Only 41 cases of recurrent ectopic pregnancy have been reported, according to Conley and Klieger[7] and an unreported case was treated on our service in 1955. Some occurred after cornual resection, others after simple salpingectomy. This is a very small number of cases, considering the frequency of salpingectomy for ectopic pregnancy. On a statistical basis, it appears that the chance of a recurrent ectopic pregnancy is so slight that there is little difference which type of operation is done.

Fig. 2.—Hysterosalpingogram following right salpingo-oophorectomy and cornual resection showing patency of the right cornu.

Evidence has also been presented which strongly suggests that regeneration can occur after resection of the interstitial portion of the tube.[7-10] In our institution, in several cases, hysterosalpingograms taken after deep cornual resection have shown patency of the resected cornu (Fig. 2). Cook and Butt[11] also demonstrated this effect but attributed it to accidental perforation of the cornu by the cannula during hysterosalpingography. In their illustration, the uterine cavity and remaining tube filled normally, which would indicate that the cannula was in the uterus, not the peritoneal cavity. Their patient suffered no ill effects, and it is quite possible that the oil passed through the cornu not because of a perforation but because it was patent, as in our cases.

Thus, it is apparent that even a complete cornual resection may not prevent a future interstitial pregnancy. Since such a procedure carries with it the danger, however slight, of rupture or placenta accreta in a subsequent pregnancy, a less extensive operation seems preferable. It is now our policy to excise only a small wedge of tissue at the cornu.

Summary

A case of placenta accreta with spontaneous rupture of the uterus at the site of a previous cornual resection has been presented. The dangers of a deep cornual resection have been discussed. To avoid these dangers, it is recommended that only a small wedge-shaped area of tissue be excised at the uterine cornu when a salpingectomy is done.

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AN ANALYSIS OF ONE HUNDRED CONSECUTIVE VAGINAL DELIVERIES FOLLOWING CESAREAN SECTION

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THE adage, "once a cesarean section, always a section," has in recent years undergone several revisions. Numerous articles[1-12] from clinics in this country and abroad have indicated a trend, in selected cases and under specific conditions, toward elective vaginal delivery of women who have previously had cesarean section.

From Jan. 1, 1953, and continuing to the preesnt, it has been a policy of the Obstetrical Service at Walter Reed Army Hospital to evaluate all patients with previous cesarean section for possible vaginal delivery. During this period 70.42 per cent of all who had had previous cesarean section were successfully delivered vaginally.

It is the purpose of this report to evaluate and analyze 100 consecutive patients from this group who were delivered vaginally after having had one or more cesarean sections.

Clinical Study

All patients with a history of previous cesarean section were channeled to a special problem clinic where they were followed at frequent intervals. All records pertaining to their previous obstetrical care were obtained in order to ascertain the indication for the previous section, the type of section performed, the postoperative course, and other pertinent data. These patients were informed that they would be allowed to go into labor and, depending upon their course in labor, would be delivered of their infant normally. They were assured that every precaution would be taken for their complete well-being and that any indicated section would be done without delay. It is a rare exception when patients do not readily adjust to this regimen, for the majority are quite anxious to deliver their babies vaginally. The prospect of another cesarean section is looked upon with disfavor by most patients.

These patients were admitted to the obstetrical ward approximately 2 weeks before term, as determined by clinical history, size of the fetus, and status of the cervix as noted by sterile pelvic examinations in the third trimester.

At the onset of labor, intravenous infusions were started, a staff physician consulted, a resident called and placed in constant attendance, and the blood bank and operating staffs alerted. Depending upon the patient's previous history and progress in labor, observation was made either on the obstetrical ward or in the operating pavilion.

Whenever possible, delivery was accomplished with outlet forceps over a median episiotomy, with the use of Trilene inhalation and Xylocaine pudendal block anesthesia and occasionally saddle block anesthesia. The second stage of labor was shortened or eliminated whenever possible.

Following delivery, the uterus was manually explored to determine the presence of any defects. The postpartum care was routine and the patient was discharged between the fourth and sixth postpartum days.

Cesarean Section Rate.—Table I shows the cesarean section rate for the period extending from January, 1949, to October, 1957. It is interesting to note that the section rate dropped significantly in 1953 when the policy was instituted of allowing patients with a history of previous cesarean section to be delivered vaginally.

TABLE I. CESAREAN SECTION RATE AT WALTER REED ARMY HOSPITAL

YEAR	TOTAL DELIVERIES	SECTION RATE (%)
(January) 1949	1,076	3.25
1950	1,195	2.76
1951	1,613	2.29
1952	1,971	2.32
1953	2,106	1.70
1954	1,997	1.25
1955	1,991	1.41
1956	1,956	1.23
(October) 1957	1,334	1.49

Indication for First Cesarean Section.—The indications for the initial cesarean section are listed in Table II. The leading causes were cephalopelvic disproportion and placenta previa. In one case the indication could not be satisfactorily determined, since the original section had been performed elsewhere and accurate data could not be obtained.

TABLE II. INDICATION FOR INITIAL CESAREAN SECTION (100 CASES)

INDICATION	NO.
Cephalopelvic disproportion	35
Placenta previa	29
Eclampsia	6
Transverse presentation	6
Prolapsed cord	5
Cervical stenosis	4
Uterine inertia	3
Hydrocephalus	3
Face presentation	2
Abruptio placentae	1
Previous manchester operation	1
Dermoid cyst	1
Anencephalic monster	1
Myomatous uterus	1
Previous subarachnoid hemorrhage	1
Unknown	1
Total	100

Number of Sections Prior to Vaginal Delivery.—Table III represents a breakdown of the number of sections each patient had had prior to vaginal delivery. Seventy-one per cent of the patients had one cesarean section as compared to 29 per cent that had more than one.

TABLE III. NUMBER OF CESAREAN SECTIONS PRIOR TO VAGINAL DELIVERY

NO. OF SECTIONS	NO. CASES	%
1	71	71
2	24	24
3	4	4
4	1	1
Total	100	100

Type and Number of Cesarean Sections Prior to Vaginal Delivery.—A special effort was made to determine how many patients had, as their initial operation, a classical cesarean section. Twenty-seven per cent had this type of cesarean section as opposed to 40 per cent who had a low cervical procedure (Table IV). The remaining cases were those in which more than one cesarean section had been performed. A review of this group showed that all sections were either of the low-flap or extraperitoneal type. No classical sections were performed in this group. The theoretical danger of rupture of the uterus in patients with classical sections prompted this analysis.

TABLE IV. TYPE AND NUMBER OF CESAREAN SECTIONS PRIOR TO VAGINAL DELIVERY

TYPE OF CESAREAN SECTION	NO. CASES
Low cervical	40
Classical	27
Extraperitoneal	4
Combination (two or more sections)	29
Total	100

Previous Cesarean Section With and Without Prior Vaginal Delivery.—In patients who had experienced vaginal delivery prior to cesarean section, one would anticipate that the incidence of repeat vaginal delivery, if this were elected, would be rather high. In this series, as shown in Table V, 43 per cent of the patients had at one time been delivered vaginally as compared to 57 per cent who had never had a vaginal delivery. Thirty-five per cent of this latter group had their initial cesarean section for cephalopelvic disproportion.

TABLE V. PREVIOUS CESAREAN SECTIONS WITH AND WITHOUT PRIOR VAGINAL DELIVERY

	NO. CASES
No vaginal delivery	57 (57%)
Prior vaginal delivery	43 (43%)
Total	100

TABLE VI. METHOD OF DELIVERY

Spontaneous vertex	43
Low forceps	49
Midforceps	4
Assisted breech	2
Breech extraction	2
Total	100

Method of Delivery.—Table VI shows the method of delivery of the 100 patients who were delivered vaginally. The manner in which they were delivered varied. Forty-three per cent were delivered spontaneously and 57 per

cent had an operative type of delivery. The 4 per cent incidence of midforceps occurred in the cases of secondary uterine inertia where delivery by forceps was elected. The 4 cases of breech delivery will be discussed in detail later.

Duration of Labor.—Fig. 1 is a graphic presentation of the duration of labor in all cases. The duration of labor was from 30 minutes to 24 hours, with an average labor of 8 hours. The largest number of patients were delivered in the first 11 hours.

No patient was in labor more than 24 hours, and those who were in labor more than 17 hours were either in desultory labor or had secondary uterine inertia. These cases will be discussed under Complications.

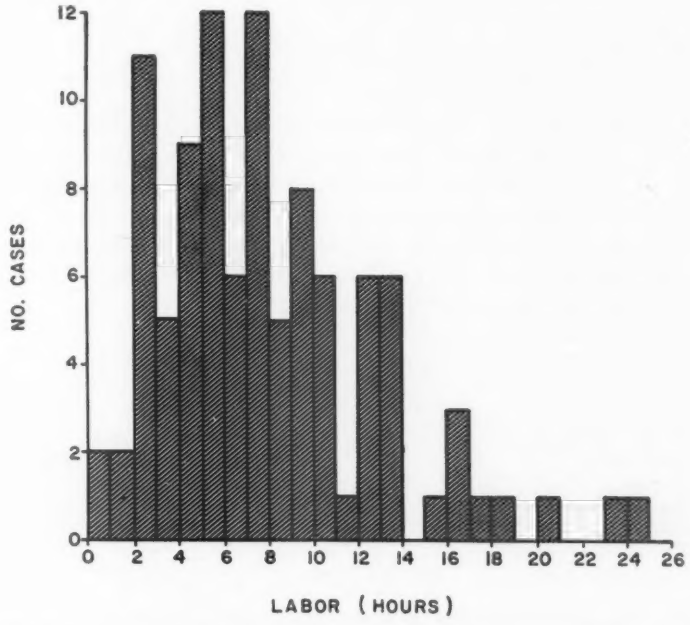

Fig. 1.—Duration of labor in hours plotted against the number of women in each group.

X-ray Pelvimetry in Patients With Cephalopelvic Disproportion Who Were Delivered Vaginally.—The 35 patients who had had initial cesarean sections for cephalopelvic disproportion and who were subsequently delivered vaginally, in most instances, had, on routine pelvimetry, an adequate pelvis. Table VII shows the distribution of measurements. The greatest percentage of patients had a Mengert index above 95 per cent. In only 9, or 25.7 per cent, of the cases was there a relative inlet contracture as denoted by an index below 95 per cent. In 4 instances, 14.4 per cent, there was a midplane contracture.

As will be discussed in the next table, the weight of the infants was a strong factor in allowing patients with a borderline pelvis to be delivered vaginally.

Comparison of the Weight of the Infants Born by Cesarean Section for Cephalopelvic Disproportion and Those Born by Vaginal Delivery.—With the exception of 6 cases, a review of infant weights showed that the infants delivered vaginally weighed less than those delivered by cesarean section (Fig. 2). The forces of labor being equal and the period of gestation similar, it is

reasonable to assume that the difference in infant weights was the factor that permitted vaginal delivery in many instances. All infants in this series of 35 patients were term.

TABLE VII. X-RAY PELVIMETRY IN PATIENTS WITH CEPHALOPELVIC DISPROPORTION DELIVERED VAGINALLY

VOLUMETRIC MEASUREMENTS (MENGERT INDEX)	INLET OF PELVIS (NO. CASES)	MIDPELVIS (NO. CASES)
65%– 75%	0	0
75%– 85%	2	3
85%– 95%	9	4
95%–105%	9	11
105%–115%	6	8
115%–125%	7	7
125%–130%	2	2
	35	35

Analysis of Complications.—Table VIII lists the complications encountered in these 100 cases. In 6 instances, a terminal uterine inertia developed late in the second stage of labor. Rather than resort to a midforceps delivery, it was elected to administer a dilute intravenous Pitocin drip in the operating room with the abdomen prepared and all in readiness for immediate cesarean section. The average duration of intravenous Pitocin therapy in these cases was 30 minutes prior to delivery.

TABLE VIII. ANALYSIS OF COMPLICATIONS (19 CASES)

COMPLICATIONS	NO. CASES	MANAGEMENT
Secondary uterine inertia	6	Intravenous Pitocin
Abruptio placentae	5	Rupture of membranes
Transverse arrest	4	Midforceps
Transverse lie presentation	2	Breech extraction
Breech presentation	2	Assisted breech delivery
Total	19	

There were 5 cases of abruptio placentae, all of which occurred in the second stage of labor. Two patients with 20 per cent separation and one with 30 per cent were delivered of living full-term infants and without incident. Two severe cases of abruptio placentae were terminated by breech extraction. In both instances, the infants weighed 1 pound, 8 ounces and 1 pound, 10½ ounces, respectively. These 2 cases represented one half of the fetal deaths in this total series.

The 2 assisted breech deliveries occurred in mothers who had a history of previous uncomplicated vaginal deliveries. In one of these cases, pelvimetry disclosed a Mengert index of 119 per cent for the inlet and 122 per cent for the midpelvis. This patient was delivered of a 9 pound, 1 ounce infant after 7 hours of labor. The other patient, with an index of 110 per cent for the inlet and 101 per cent for the midpelvis, was delivered of an 8 pound, 5½ ounce infant after 4 hours of labor.

There were 2 cases of postpartum hemorrhage, one secondary to uterine atony, and the other secondary to a retained placenta. In 6 cases only was it necessary to remove manually either an unseparated or trapped placenta. The 2 cases of uterine hemorrhage were included in these 6 cases.

There were 2 cases of postpartum thrombophlebitis, both in patients who had had vascular trouble during their previous pregnancies.

TABLE IX. FETAL MORTALITY

INFANT	DEATH	METHOD OF DELIVERY	WEIGHT		CAUSE
			POUNDS	OUNCES	
1. Premature	Neonatal	Spontaneous	3	6	ABO incompatibility
2. Immature	Neonatal	Breech extraction	1	8	Abruptio placentae, diabetes mellitus
3. Immature stillborn	Antepartum	Spontaneous	1	3	Unknown
4. Immature stillborn	Intrapartum	Breech extraction	1	10½	Abruptio placentae

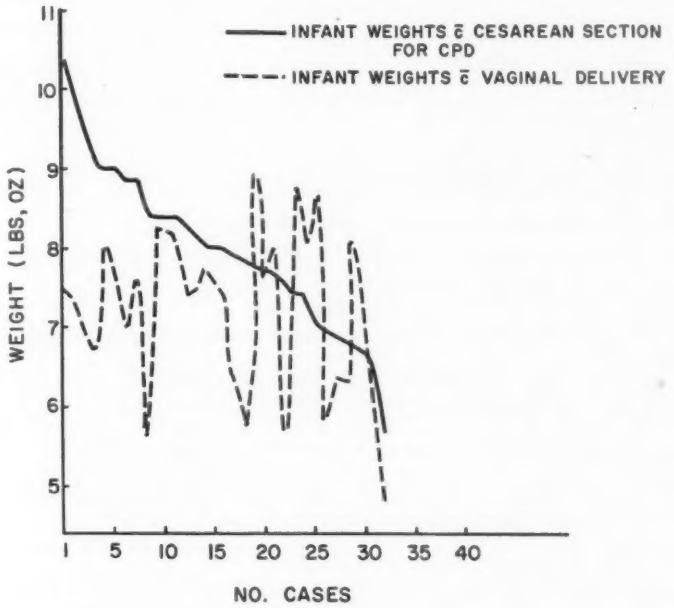

Fig. 2.—Comparison of weights of infants born by cesarean section for cephalopelvic disproportion and by vaginal delivery.

Incidence of Uterine Defect.—Following delivery, all patients had a manual exploration of the uterus. No occult or frank ruptures of the uterus were detected, and in only 20 per cent of the patients could an indentation along the line of the previous incision be palpated.

Fetal Mortality.—The uncorrected fetal mortality rate was 4 per cent. Table IX shows that this mortality rate could be justifiably corrected to zero.

There was no maternal death in this series.

Conclusion

The adage, "once a cesarean section, always a section," does not, in modern-day obstetrics, have the same connotations it formerly had. Repeated violation of the anterior paries and pregnant uterus can be prevented in many cases of previous cesarean section by proper and complete clinical, physical, and radiological evaluation of the patient.

Summary

1. One hundred consecutive vaginal deliveries in women who had had previous cesarean section have been analyzed. This group of patients represented 70.24 per cent of all previous cesarean section cases seen in a 5 to 6 year period.

2. Forty-three per cent of this group had been delivered vaginally one or more times as compared to 57 per cent who had never experienced a vaginal delivery.

3. Thirty-five per cent of these patients had their initial section for cephalopelvic disproportion. The weight of the infants played a role in allowing for successful vaginal delivery. In 77 per cent of the cases, the infants delivered vaginally weighed less than those delivered by cesarean section. In most cases, pelvimetry studies in this group disclosed an adequate pelvis.

4. Complications were minimal with no frank or occult rupture of the uterus encountered.

5. There was no maternal death in this group and all fetal mortality could be corrected.

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CESAREAN SECTION IMMEDIATELY FOLLOWED BY RADICAL HYSTERECTOMY AND PELVIC NODE EXCISION

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PREGNANCY complicated by cancer of the cervix is rare. Several reviews on this subject have been published and in a recent one by Marcus, Brandt, and Cibley[2] the frequency of this coincidence is given as varying between 0.02 and 0.05 per cent. Thus no one author may claim much personal experience with such cases. For obvious reasons the management will depend upon the stage of the pregnancy and also the stage of the cancer when first seen.

It is our opinion that when radical surgery can be carried out to its fullest extent under optimum circumstances, this form of treatment offers the patient the best chance for cure of carcinoma of the cervix. There is no reason to modify this view in the event of coexisting pregnancy in any stage.

The purpose of this report is to record an instance of cancer of the cervix complicating late pregnancy and treated by classical cesarean section immediately followed by radical hysterectomy and pelvic node excision, *as this operation has been described by the senior author.*[1]

Case Report

C. D., aged 34 years, para ii, first noted painless postcoital bleeding in November of 1956. This bleeding was again observed in March, 1957. In May, 1957, the obstetrician noted a cervical lesion that bled easily. In July, 1957, cervical smears were reported as showing malignant cells and two weeks later a biopsy revealed epidermoid carcinoma.

In late August, 1957, she was first seen in the outpatient clinic of the Memorial Center. Pelvic examination revealed an ulcerating carcinoma *about 2 cm. in diameter* on the left portion of the portio with induration of the adjacent left parametrium and questionable tightness of the left uterosacral ligament near the cervix (Stage II). The uterus was enlarged to a size consistent with 24 weeks' pregnancy. The last menstrual period was stated to have been Feb. 20, 1957.

She was admitted to the Memorial Center for routine studies which included blood chemical analyses, chest films, and intravenous pyelograms, all of which were normal. Pelvic examination confirmed the original findings. The question was raised as to treatment by hysterotomy and then radiation, with radical surgery 6 weeks after radiation. It was finally decided to pursue expectant treatment for about 8 weeks and then carry out cesarean section followed immediately by radical hysterectomy and pelvic node dissection in order to secure a viable baby under favorable circumstances. She was discharged after 3 days and followed as an outpatient.

She was admitted to the New York Lying-In Hospital on Oct. 28, 1957, for operation because of facilities for newborn infant care, and the operation was performed on Oct. 31, 1957. Preoperative pelvic examination revealed a slight but definite increase in size of the lesion, and left paracervical induration. It was still unquestionably a Stage II lesion.

General anesthesia was employed with Pentothal induction. After the birth of the baby, hypotension was induced with Arfonad in combination with Anectine and curare. An intravenous infusion was started preoperatively by cut-down in the left ankle, and a Foley catheter was placed in the bladder.

Through a midline incision extending downward from the umbilicus a high classical cesarean section was carried out, producing a vigorous male infant who weighed 3,100 grams. The placenta and membranes were removed manually, and the uterus closed with continuous No. 2 chromic catgut. Five minutes elapsed between the time the anesthesia was begun and the placenta and membranes were delivered; oxytocin was injected after the placenta was removed.

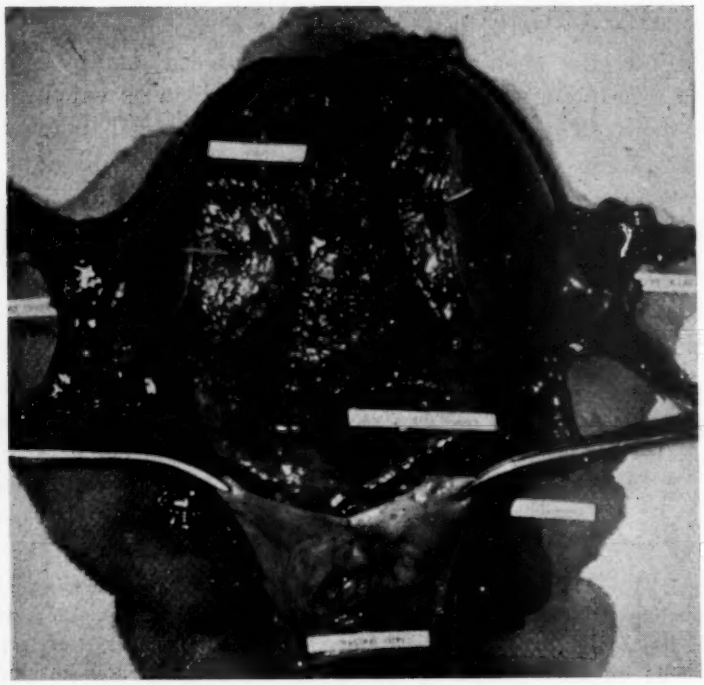

Fig. 1.—Postoperative specimen of uterus excised by Wertheim type radical hysterectomy and large vaginal cuff. Note attached parametria and cancerous cervix.

The patient was placed in deep Trendelenburg position and the lower portion of the abdominal wound extended downward. Both infundibulopelvic ligaments were doubly clamped and transected as were both round ligaments close to the abdominal wall. The pelvic peritoneum overlying the external iliac and common iliac vessels on both sides was incised between the stumps of the infundibulopelvic ligament and the stumps of the round ligaments. The nodes and areolar tissues over the common and external iliac vessels were excised. The areolar tissues between the layers of the right broad ligament were reflected mesially.

The uterine arteries were secured at their origin, doubly clamped, and ligated. The uterine veins were similarly secured. The peritoneal reflection between the bladder and vagina was incised transversely and the two separated for a considerable distance downward. The ureters on each side were identified and freed from the "tunnels" in each broad ligament down to their entrances into the bladder.

Fig. 2.—View from above of "skeletonized" pelvis following radical hysterectomy and pelvic node excision. *B*, Bladder retracted forward and upward. *U*, Ureters. Note denuded pelvic floor on each side.

Fig. 3.—View of right side of pelvis after radical hysterectomy and pelvic node excision. The right ureter is retracted upward showing denuded right pelvic wall. *O*, Obturator nerve. *N*, Exposed roots of right sciatic nerve after excision of hypogastric artery and vein. *E*, Margin of peritoneum remaining after deperitonization of pelvis carried out during the course of the operation.

Induration in the left parametrium, extending about 3 cm. away from the left side of the cervix, and in the left uterosacral ligament, extending about 2 cm. backward from the cervix was noted. The uterosacral ligaments were transected well backward at the levels of the lateral aspects of the rectal walls.

The peritoneal reflection at the bottom of the cul-de-sac of Douglas was incised transversely and by blunt dissection the rectum and posterior vaginal wall were separated downward for a considerable distance. The vagina was transected about 4 inches from the cervix, and the uterus, appendages, and adherent parametria excised (Figs. 1 and 2).

The right internal iliac artery was doubly clamped and transected about 1 cm. distal to the bifurcation of the common iliac. Perforating branches toward the greater sciatic notch were clamped and ligated. The fatty tissues and nodes in the obturator fossa were separated mesially from the pelvic wall and the obturator artery and vein transected and ligated just before their entrance into the obturator canal. The obturator nerve was freed from surrounding tissues and left in situ. The hypogastric vein near its junction with the external iliac vein was isolated, doubly clamped, and ligated. Its branches perforating backward between the roots of the sciatic nerve were transected and ligated.

As forward traction was exerted on the distal segments of the internal iliac artery and vein, adherent fatty tissues and nodes were carried with them and the sciatic nerve roots exposed. The hypogastric vessels and tissues were then excised (Fig. 3). Two 2 inch gauze packs were then tamponed lightly against the sciatic nerve roots, one on each side, and the ends pushed into the vagina.

The greater omentum was pulled downward and its right half divided from the attachment to the transverse colon forming a long omental apron. This was pushed deeply into the left pelvis and the end brought across to the right under the ureters and then back over the ureters to the left and sutured in this position. A large flaccid omental tube was thus fashioned to surround the lower ureters, in an effort to obviate ureteral fistula.

During the operation the systolic blood pressure varied between 55 and 80 and the diastolic between 35 and 50 mm. Hg. Most of the time the blood pressure was steady at 60/40. A total of 3,000 c.c. of whole blood was given during the operation. A seventh unit (500 c.c.) was started as the patient left the operating room.

Pathologic study disclosed squamous-cell carcinoma of the cervix with invasion of paracervical tissue. There were no metastases in the tubes or ovaries. Seven nodes from the right side were sectioned and ten nodes from the left side; all were negative for metastases.

The postoperative course was essentially uneventful. The maximum temperature was 100.2° F. (rectal) on the sixth day. The pelvic packs were removed under Trilene anesthesia on the fourth day. Intravenous pyelograms on the thirteenth day showed slight hydronephrosis. The catheter was removed on the eighteenth day. Mother and infant were discharged on the twenty-third day, the latter weighing 3,370 grams. Subsequent examinations have revealed both to be progressing satisfactorily.

Comment

From the patient's history, it is probable that conception occurred after inception of the cervical cancer.

Radiation was not employed in order to protect the fetus from injury. Time was lost during the two months' observation period; the lesion did increase slightly in size but remained in Stage II. No nodal metastases were detected in study of the specimen.

The management of this particular case may be open to discussion and only time will reveal whether the carcinoma has been eradicated, but certainly the safety of the child was protected. The price necessarily paid for maximal protection of the fetus was the 2 months' delay in attacking the carcinoma.

The point is made in this report that a radical panhysterectomy with pelvic node dissection is feasible immediately following a cesarean section at the thirty-second week of pregnancy.

We wish to express appreciation to Dr. R. Gordon Douglas for making available the facilities of the New York Lying-In Hospital. His resident staff, Dr. Ben Marbury (Anesthesia) and Dr. Roy Bonsnes (Laboratories) made possible the care of this patient and the preparation of this report.

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RELATION OF MATERNAL MORTALITY RATES TO ALL DEATHS ASSOCIATED WITH CHILDBIRTH

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(From the Brooklyn Committee on Maternal Welfare)

EARLY inquiry into the causes of maternal deaths in the United States was "especially stimulated by progress of the movement for reduction of infant mortality,"[1] when investigation had shown a direct relation between infant mortality and the steadily rising number of deaths due to puerperal causes. In this first important report, maternal mortality and puerperal mortality as terms of reference were used interchangeably. In this study and the next,[2] only deaths due to pregnancy and childbirth were classified as puerperal.

Deaths to which puerperal conditions contributed, yet not decisively, were not included. Deaths due to criminal abortion were excluded and assigned to homicide, and it was pointed out that "frankness on the part of physicians and zeal on the part of public authorities in investigating deaths thought to have resulted from criminal abortion, and in correcting the certificates for the deaths would reduce the number of deaths assigned to puerperal causes."[2] The deaths from self-induced abortion were included grudgingly, since it was felt that this should not be considered part of the risk of death to which expectant mothers were exposed.

The early definitive studies made in New York[3] and Philadelphia,[4] initiated because "statements have never been backed by carefully collected and studied statistics," took into account all the deaths associated with pregnancy whether directly due to complications of pregnancy or not. An important report from Cleveland[5] at about that time said that inclusion of abortion, toxemia in the first trimester, ectopic pregnancy, and intercurrent disease had done a serious injury to the cause of obstetrics. Siegel,[6] in a report from Buffalo, labeled as fallacy the inclusion of abortion and ectopic pregnancy. Skeel,[7] defining as puerperal all deaths following delivery and the "mishaps of early pregnancy," wished to consider maternal mortality as a delivery death rate, excluding death which occurs with any form of birth of a previable fetus.

In 1950 we were told[8] that the 1949 maternal mortality rate was below the apparently irreducible minimum and had become a purely local problem. And in 1956 it was said that "our goal . . . can no longer be centered primarily on vital statistics and physical survivial of mothers and infants . . . but on an emotionally secure family environment,"[9] presumably from the cradle to the grave.

Jewett,[10] speaking for the Massachusetts Committee on Maternal Welfare, takes vigorous issue with this point of view, pointing out that the proportionate causes of maternal death have not changed; and in Michigan,[11] where preventability is stressed, they believe that such complacency is unwarranted and dangerous.

The basis for calculation of the maternal mortality rate is the number of deaths assigned to deliveries and complications of pregnancy, childbirth, and the puerperium. Prior to 1949 there were rigid rules for priority when more than one cause was reported, as is common. At present the cause named by the certifying physician is the one tabulated. The program for review of maternal deaths remains confused, however. There is an effort to compromise the situation by separating death into compartments called puerperal or direct, nonpuerperal or indirect, and nonrelated. There is no good reason for this division which but serves to lessen the interest of the obstetrician in many important causes of maternal death.

In Brooklyn, New York, maternal deaths have been continuously studied since 1934. Assignment of preventability was quickly abandoned and controllable factors of death elaborated. Since 1936 certificates of all deaths associated with pregnancy have been matched with case reports and freely discussed in large meetings open to every physician in Brooklyn.

In New York City the physician's confidential report, part of the certificate of death, includes a question asking if pregnancy had occurred within six months of death, and if so, the date of delivery. All terminated pregnancy no matter how early is reportable. It is felt that very few deaths associated with pregnancy are missed.

Material for Study

As part of our continuing investigation into the association of pregnancy and heart disease,[12] but principally to discover the true importance of review of all deaths associated with pregnancy, 403 cases for the period 1949-1956 have been analyzed; 1949 was selected because it was the first year in which all causes were coded according to the sixth revision of the International Lists.[13] Possible alternatives in treatment and controllable factors were determined in group discussion. All the deaths associated with pregnancy are shown in Table I.

TABLE I. DEATHS ASSOCIATED WITH PREGNANCY

YEAR	PUERPERAL OR DIRECT*	NONPUERPERAL OR INDIRECT	LIVE BIRTHS
1949	48	25	57,716
1950	41	22	56,464
1951	32	20	58,389
1952	30	17	57,932
1953	30	10	55,851
1954	23	10	56,106
1955	34	14	56,680
1956	31	16	56,873
Total	269	134	456,011

*For calculation of maternal mortality rate.

TABLE II. OFFICIAL ASSIGNMENT OF MATERNAL DEATH

CAUSE	NO. OF CASES
Abortion	60
Dystocia	7
Ectopic	21
Hemorrhage	88
Infection	36
Toxemia	57
Total	269

For the most part it was easy to fit the official maternal deaths into the usual familiar table. Seven deaths officially coded as caused by dystocia could not be tabulated otherwise, however.

Abortion accounted for 60 deaths, 22 per cent of all the maternal deaths; 46 of these women were non-white. Two women died of hemorrhage, and 2 from anesthesia for curettage. In all but 4 cases, abortion was septic and thought to have been induced. The failure of antibiotics was perhaps due to the patients' delay in seeking treatment. Other than in abortion, however, the number of deaths due to infection (36 cases) is notable in the light of present-day confidence in antibiotics.

In ectopic pregnancy the principal controllable factor was late treatment or none at all. One woman was found dead at home, 3 died on the way to the hospital, and 2 women died shortly after admission. Death was due to infection in 2 cases, and in 2 cases to anesthesia.

Hemorrhage was the cause of death in 88 cases, and caused death in an additional 19 cases (abortion 2 and ectopic pregnancy 17). Lack of blood replacement was not so much a factor in death as unawareness of the primary importance of prevention and limitation of blood loss. Other than delay in transfusion of blood or administration of inadequate amounts, controllable factors were associated with anesthesia, rupture of the uterus, incompatible blood, afibrinogenemia, acute renal failure, delivery of the fetal shoulders, breech and scapular presentations, twins, version, antepartum anemia, Pitocin induction, retained placenta, hemorrhage during cesarean section, and even episiotomy.

In sepsis, hemorrhage was often considerable. In toxemia, delay in hospitalization and cesarean section were controllable factors.

Anesthesia

In no review of maternal deaths is it possible to discover the importance of anesthesia other than by scrutiny of case records. The certificate of death may clearly state that death was due to an explosion during administration of anesthesia or to aspiration of vomitus, or that it occurred suddenly shortly after regional block, yet the statistician is instructed to code death to therapeutic misadventure (E954 or N999.2[13]) but only when the primary condition is unknown. He may assign it to asphyxia (795.0[13]) or possibly to heart block (433.0[13]).

Actually, 31 deaths were due to anesthesia. Seven of these, all in the course of cesarean section, were not coded as maternal deaths but were assigned to diabetes, pneumonia, nonpuerperal embolism (2 cases), and heart disease (3 cases). The other 24 deaths were coded as maternal mortality under the following rubrics: dystocia (11 cases), toxemia (2 cases), abortion (2 cases), placenta previa (2 cases), ectopic pregnancy (2 cases), infection (1 case), asphyxia (3 cases), and therapeutic misadventure (1 case). Anesthesia was general in 18 cases, and regional in 13 cases. Cesarean section was performed in 17 cases. Controllable factors concerned the anesthetist.

Nonpuerperal or Indirect Causes of Death

There were 134 deaths associated with pregnancy that were not coded as maternal mortality. For each of the following diagnoses there was but one death: amyloidosis, cerebral hemorrhage, hepatic cirrhosis, Hodgkin's disease, hepatitis, lupus, rupture of an aneurysm of the splenic artery, pituitary disease, thyrotoxicosis, and phosphorus poisoning. Death and pregnancy are, as might be expected, more closely related to the indirect or nonpuerperal causes commonly reported in Table III.

TABLE III. DEATHS FROM COMMON NONPUERPERAL CAUSES

CAUSE	NO. OF CASES
Rheumatic heart disease	40
Other heart disease	14
Carcinoma*	21
Operations†	14
Cerebral aneurysm	5
Sickle-cell anemia	4
Poliomyelitis	4
Tuberculosis	4
Nephritis	4
Diabetes	4
Asthma	3
Epilepsy	3
Pneumonia	2
Pancreatitis	2
Total	124

*Chorionepithelioma, 2 cases.
†Acute appendicitis, 5 cases.

Heart Disease.—Statistically heart disease includes all forms except syphilitic and thyrotoxic. The importance of its association with pregnancy as a cause of death cannot be shown by statistics. In Brooklyn from 1937 to 1949 heart disease, other than rheumatic and congenital, was mentioned on 62 certificates of death, yet in 42 cases (67 per cent) a diagnosis of heart disease was not borne out by the case report.[12]

During that period 66 per cent of the deaths in which pregnancy and childbirth were joint causes were coded to maternal mortality, and 34 per cent to heart disease. Since 1949, in 46 cases, 6 (13 per cent) were coded to the maternal death rate and 40 (87 per cent) to heart disease.

It is particularly difficult to discover the frequency of hypertensive heart disease, largely because of its relation to the toxemias of pregnancy. Congenital heart disease caused death in 2 cases, and in one case coronary occlusion was found at autopsy. Heart disease accounted for 40 per cent of the nonpuerperal causes of death, helping considerably to lower the maternal mortality rate.

Rheumatic heart disease: Rheumatic heart disease contributed to death in 46 cases; 19 women were undelivered. Six cases were coded to puerperal causes, yet in each case death was due to congestive failure. But for a few deaths attributed to pulmonary embolism, heart failure was a consistent cause of death. Controllable factors were found in the quality of antepartum care, time of hospitalization, intravenous fluids, and cesarean section.

Since the effect of concurrent age and parity cannot be known other than by maternal death studies, it is shown in Table IV.

TABLE IV. AGE AND PARITY OF PATIENTS WHO DIED FROM RHEUMATIC HEART DISEASE

AGE IN YEARS	TOTAL CASES	PARITY					
		0	i	ii	iii	MORE THAN iii	NOT STATED
20-24	17	11	5				1
25-29	8	6	1		1		
30-34	9	3		4		1	1
35-39	5	1	1	1		1	1
40-45	7		1	2	1	3	
Total	46*	21	8	7	2	5	3

*Includes 6 coded to maternal mortality.

Comment

When all the deaths associated with pregnancy in Brooklyn during the period 1949-1956 were reviewed, it was found that 269 had been officially coded to the maternal mortality rate as direct causes of death. During this period 134 deaths associated with pregnancy were not included, a few of which occurred 3 to 6 months after the termination of pregnancy. Caused by so-called nonpuerperal or indirect factors, some of these deaths may be unrelated to the risks of childbirth.

It should be clear that there is no sharp line of demarcation between the direct and the indirect causes of death. Obviously the maternal mortality rate has many useful applications, but the rate itself is not our target. The object of our concern is all the women who die of whatever cause during pregnancy, and within an arbitrary period of time afterward. McKelvey[14] sees no reason why we should follow old rates, and suggests a 3 months' period of time afterward. He would exclude only the deaths which appear to have had no connection with the obstetric event. Ross[15] makes no exceptions, suggesting a 6 months' time period.

By 1946 it had become clear that hemorrhage was the first cause of maternal death,[16] and we are often told that heart disease is the fourth cause, but this can be shown only by inclusion of deaths outside the statistical classification of maternal mortality. To learn the causes of mortality is not enough, however. We must know the circumstances of each death, if we wish to discuss alternatives and controllable factors.

When the mortality associated with childbirth is coded directly to rheumatic heart disease, a large number of cases escape tabulation as maternal deaths and obstetric study committees may be unaware of them. Similarly, the internist must know the number and circumstances of these deaths. This knowledge can be had only from maternal death studies which include all the deaths associated with pregnancy and childbirth.

Statistics but outline the problem. When extended by case reports they open the door to the group discussion or obstetric conference which holds its solution. Its purpose is not to inform, but to teach. Here knowledge of the swift onward march of research may be exchanged, and spread to where it can do the most good. Now that obstetrics is given less time in the undergraduate curriculum this form of education grows in importance. As a practical teaching mechanism the analysis committee is nearly perfect, and it would be perfect if

all engaged in the teaching and practice of obstetrics should participate. Showers of statistics however desirable can never have the impact which accompanied the publication of early studies.

There is still room for education of the public. Women appear to be ignorant or careless of the risk in abortion. And the expert statisticians who will soon rewrite the International Lists of Diseases and Causes of Death need education too. Anesthesia is of the utmost importance as a cause of maternal death if only because so much can be done about it. The present classification makes no provision for it. It is time it did.

Perhaps because we live in an age of conformity, or are obsessed with what we rather complacently think of as a program, preventability is still widely assigned. There is, however, a concert of effort to minimize "preventability (avoidability) . . . it should be judged in an ideal academic sense."[17] Preventability never was the right word since it implies successful anticipatory action, yet it did give decisive impetus to the attack on the high maternal mortality rate. Thus, a generation ago, compulsion of events forced obstetricians to accept a term completely remote from their traditions. It is not easy to recapture the atmosphere of those vanished years, yet I can testify that there was no indication of superior knowledge by the members of the committee which first met the crisis.[3] Assignment of preventability is an idle, irritating custom which serves no useful purpose.

There is no lack of work for committees on analysis to do. There are, however, two major weaknesses in contemporary practice—failure to review all the deaths associated with childbirth and assignment of preventability. Both have their roots in an attitude toward maternal mortality which is essentially sterile.

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32 Remsen Street

DEPARTMENT OF CURRENT OPINION

Pertinent Comments

ANNOUNCEMENT

THE AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY wishes to announce the initiation of a new feature entitled "The Department of Current Opinion."

The present Editors are keenly aware of the growth in stature of this JOURNAL over the years, based on its honest and conservative devotion to factual presentations. Studies which have been thoughtfully carried out have been, in these pages, directly presented. These studies might deal with a recurrent distressing clinical problem; they might concern themselves entirely with physiologic research which apparently had no immediate clinical application; but in each instance the factual background of the investigation has been carefully evaluated and presented.

Neither the JOURNAL nor its Editors would for one minute yield a single iota of this reputation for having important unbiased observations recorded within these covers. Yet each of the Editors has been desirous of finding an avenue for the equally able presentation of opinion. If the author of every paper is to be scrupulously confined to the factual reporting of his investigation and his observations, wherein do these (or other) authors find an avenue for their individual comments, their critical thoughts?

The Department of Current Opinion will be as valid as the scientific papers accepted by the Editors, but the validity will be one of opinion and thought, without the documented factual background characterizing the remainder of this JOURNAL. Thus, for example in a scientific report, an investigator would be required to refer to THE AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY 75: 718, 1958, whereas in the pages of The Department of Current Opinion this same writer might refer affectionately to the GRAY JOURNAL.

Specifically, this Department will contain three subdivisions, which will be presented in approximate rotation. These three subfeatures will be entitled: Pertinent Comment, Re-evaluation, and Clinical Problems.

Pertinent Comment

Here will be found those remarks which lie midway between the "Comment" portion of a formal paper, and the "Editorial" of the traditional journal approach. Matters of significance may be discussed; trivial subjects will be reviewed. The trends of medicine in general and our speciality in particular will be commented on—without syllogistic proof, without presentation of masses of data, and (we hope) without pomposity. Many letters to the Editor might well fit into this category, as might many informal editorials. Differences will be aired, but acrimony will not be supported. Intelligent and clever debate is welcomed; destructive criticism will be shunned. Here the passing medical scene, with its serious aspect and its foibles, will be for a moment immobilized, to just the extent that the passing scene can ever be so captured.

Re-evaluation

Many authors who contribute to this or to other journals in our speciality offer to their readers a small and select number of papers, widely spaced in time and conveying finished concepts, accomplished facts. These contributions are tremendously worth while, but are not always immediately exciting. Other writers will describe more exciting concepts which are still in the process of development. The average reader cannot always know the ultimate practice or the current belief of the writer who has reported his work in progress.

In 1955 Dr. Roe may have claimed that the North African bullfinch was the best of all assay animals for pregnancy tests, yielding a result which was 100 per cent accurate. In 1958 does Dr. Roe still import the North African bullfinch for his day-to-day pregnancy tests? And if not, why not? Does Dr. Doe still endorse the technique he advanced (on the basis of 5 cases) for the closure of ureteral vaginal fistulas? And what of Dr. Moe and his revolutionary views anent vaginal hysterectomy? Here, in this section of the Department of Current Opinion, the writer will have the opportunity of reviewing his previous comments and may either endorse them, modify them, or retract them as he may wish. To the reader will be given the opportunity of discovering precisely what the writer may actually practice at the current moment.

Clinical Problems

Every clinician facing the immediate necessity of treating sick people has a "problem case." His particular patient may not display all the clinical features listed in the latest erudite paper on this general subject. What can he do for this woman? What are the immediate steps he should take? "Clinical Problems" is a consultation service designed to bridge this gap between the authority who writes on technical details and the practitioner with an immediate problem. What should one do at this point? Where does one turn next?

The section on Clinical Problems which will appear every third month in this new Department is designed to answer these questions. Actual cases will be discussed; each will be carried to its crucial point, and then submitted to a

consultant. Their answers may be in total conflict, and are not guaranteed to be the final word from Delphi; but their answers will be in most instances helpful to the practitioner with the problem case.

That journal—scientific or otherwise—which ignores reader reaction and still succeeds has not yet been published. The Reader Survey conducted a few years ago by the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY indicates the awareness of the Editors of the preferences and opinions of our readers. It is stating the obvious to point out that in establishing this new Department it is the belief and the hope of the Editors that it will prove both helpful and interesting. It will appear after the formal scientific papers and before Reviews and Abstracts. One might even anticipate that regular readers would develop the habit of turning first to these pages of the GRAY JOURNAL.

H. C. T., Jr.
J. I. B.
A. C. B.

THE EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES (E.C.F.M.G.)

THE number of residency appointments annually available in the United States for postinternship training is approximately twice the number of men and women annually graduating from our medical schools. Under such circumstances it is inevitable that many of these appointments go unfilled, and the spectacle of foreign-trained physicians occupying residency positions in our hospitals has been an increasing phenomenon during the past few years. Currently more than 6,000 foreign-born and foreign-educated men and women hold intern and residency appointments in the United States.

Within the past few months the American Medical Association, the American Hospital Association, the Association of American Medical Colleges, and the Federation of State Medical Boards of the United States attacked this problem of the foreign-trained applicant for residency training in this country. Acting through the Educational Council for Foreign Medical Graduates (E.C.F.M.G.), they propose to administer to these physicians qualifying examinations in an effort to achieve a system of standard ranking. These examinations, not unlike those of the National Boards in type, will be administered in the applicants' own country, and it is contemplated that in the future the hospitals in the United States will have available some impartial indication of the candidate's knowledge and ability, prior to appointing him.

Complex and difficult as this globe-wide examination system would seem to be at first glance, there can be little doubt that—if it works as visualized—this will be a great step forward. Unable to demand personal interviews in most of these cases, the hospital or chief of service contemplating the appointment of foreign physicians to residency positions has, in the past, been forced to gamble, and this gamble has often not worked out well for the hospital involved. Many embarrassing and difficult situations should be avoided, thanks to the E.C.F.M.G.

Unfortunately, however, this unravels only half of the problem, and the question immediately arises, "Who will qualify the residency vacancies and certify them to the candidates?" One cannot ignore the fact that for each episode of a poor physician lowering the quality of a good residency program, there is the equally distressing situation of the competent and intelligent foreign graduate finding himself in a marginal residency appointment. While the Council on Accreditation maintains an inspection and approval system, this is not always available to the candidate, who is apt to rank "training in America" as desirable, without fully understanding the nuances of the data listed in the J. A. M. A. The distinction between the training programs available in Hickory Corners General Hospital and the Massachusetts General Hospital may not always be clear to all candidates.

The unfortunate aspects of such confusion are not entirely personal; do not completely afflict only the individual resident who finds himself in Hickory Corners General doing the mundane work of the moment without a true postgraduate curriculum being available. This unfortunate situation is not entirely individual in its impact because many of these trainees are the potential leaders of medicine and medical thought in their respective countries. They have had the initiative to travel far for additional training; they are eager, aggressive, and in most instances intelligent. Through the barrier of different manners, a strong accent, and a strange tongue, one can see future leaders. The burning question is: What will these leaders think of America's postgraduate medical training if they have seen only Hickory Corners General Hospital?

The answer to this question is, of course, readily obtainable. One has only to travel in West Germany and talk informally with the physicians who are under 45. Their concept of American resident training programs in obstetrics and gynecology, for example, is incredibly poor; and when these concepts are traced to their origins it turns out that Herr Doktor So-and-So once took a year of training in America and he says (with contempt) that resident training is conducted in such-and-such a fashion. And when one traces still further, Herr Doktor So-and-So spent this year (after which he had the good sense to resign) in a marginal residency program. So goes our current reputation in many countries of the world.

One cannot help but admire the Educational Council for Foreign Medical Graduates for undertaking this ambitious testing program. The ranking of European candidates for our residencies will be of immeasurable help to many department directors, many hospital administrators. But should not these directors and administrators also take examinations, the results of which would be available to the candidate who seeks training in this country?

A. C. B.

CONSERVATION OF POSTPARTUM NURSES' TIME—BEDSIDE SELF-MEDICATION AND PATIENT CONTROL OF VISITING

HOWARD P. TAYLOR, M.D., CLEVELAND, OHIO

(From the Department of Obstetrics and Gynecology, The Cleveland Clinic Foundation, and The Frank E. Bunts Educational Institute)

A RECENT survey in Cleveland Clinic Hospital revealed that in one week 63 hours of graduate nurses' time was required to prepare, pass, and record routine medications given to ambulatory puerperal patients; an estimated additional 44 hours was consumed in policing visitors; thus a total of 107 hours was spent in services that more often than not brought forth unfavorable remarks or complaints from the patients or their families. Examples of these remarks are: "Nurse woke me last night to ask if I needed a sleeping pill," or, "Nurse forced me to take a sleeping pill when I wanted to watch the late movie on television," or, "It took Nurse more than an hour to bring me an aspirin for my headache," or, "My husband had a fight with that 'battle-axe' over your silly visiting regulations." Such complaints are threats to good public relations, emphasize the human problems in the nursing profession, and constantly place the doctor in the middle, between patient and nurse, in unresolved situations. Under these conditions everyone loses face.

Continuous, unrelieved shortage of nursing personnel causes a dire chain reaction. Obstetric care becomes dangerously hampered, much-needed hospital facilities have to be closed to the public, patients become dissatisfied with hospital care, there is a noticeable loss of morale among the nurses with frequent resignations, and discontent and discord arise among members of the medical staff.

What can be done to offset these consequences?

While waiting—with little hope of early success—for wiser heads to solve the vexing problems of nurse procurement, it is possible to institute physical arrangements and revised nursing procedures to provide safe and adequate patient care as well as to produce a professionally stimulating environment for nurses and doctors. A constant-care room, early controlled ambulation, shower baths, and modified rooming-in procedures for the patient, all conserve precious hours of nurses' time and at the same time give the patient a much-needed feeling of confidence and self-sufficiency. On-the-job training for the practical nurse and nurse's aide broadens the scope of their usefulness, and utilization of medical students for nursing duties during the evening hours achieves better distribution of thinly spread graduate-nursing personnel. By permitting bedside self-medication and family control of visiting, the only remaining available

source of manpower, that is, the patients and their families, may be tapped. The nursing work load will be further lightened as simultaneously the benefits of patient participation are subtly obtained.

Two recent innovations at our hospital have resulted in such widespread patient acceptance and nursing approval that we feel warranted in presenting them in this report. They are *bedside self-medication* and *patient control of visiting*.

To start with, standardized postpartum routine medications were agreed upon by the Obstetric Staff. They consist of: mineral and vitamin capsules, two each day; AACaffiene as a general pain pill; a bedtime sedative; a laxative; and a nipple cream. Sufficient medication for seven days is packed in bottles, plainly labeled by name, purpose, and directions for administration.

When the patient is moved from the Constant-Care Room to her permanent room, the nurse presents her with an attractive plastic tray containing the standardized medications. Full explanation of the self-medication is accomplished in a few minutes. By agreement with medical, nursing, and administrative staffs no record of these medications is required. Under these arrangements special medications, such as antibiotics or narcotics, are immediately administered by nurses. The patient is encouraged to take the medications as needed very much as though she were in her home environment. Knowledge of the immediate availability of medication has proved to be extremely reassuring to the patient. As a result, we have decreased the use of narcotics by two-thirds, the use of bedtime sedation by one-half, and totally eliminated complaints! Moreover, our nursery nurses have observed that they now rarely see a "dopey" baby.

One of the commonest causes of the hospitalized patient's unhappiness is due to unimaginative visiting restrictions. We are attempting to be realistic in our program. At the time of delivery the father is given a "Father's Visiting Card" entitling him to admission during each visiting period. After delivery both parents are given a pad of Visitor's Passes with instructions to fill out the passes with the names of expected visitors, give them to the ward secretary, who sends them to the visitor's desk in the main waiting lobby of the hospital. The doctor reminds the patient that she, as an intelligent person, should fully realize that she will not obtain the complete benefit of her hospital stay if she becomes tired from excessive visiting and, moreover, that she should consider her roommate and not involve her in tiring procedures. Patients have cooperated to such an extent that there has been a marked decrease in the number of visitors. No longer do we have visitors sneaking up the back stairs in violation of regulations; no longer do our nurses dread visiting hours; and the doctors are not disturbed by telephone calls at home by irate relatives who complain that they were not admitted to see the patients.

The majority of hospital obstetric patients are healthy young women undergoing a normal physiologic process. A few years ago these women would have remained at home for delivery, for then only the abnormal cases were thought worthy of hospitalization. Hospital routines were established to care primarily for the abnormal cases, with little or no thought given to establishing routines for the care of the majority of our patients, normal puerperas. In reality

the hospital should be considered as an extension of the patient's home, where she and her husband in safety may share the reproductive experience; where, under expert medical and nursing supervision, mother, father, and infant may sink the taproot of family living which is the basis of family growth and solidarity.

This philosophy can succeed if it is shared by administrative, nursing, and medical staffs, and requires that:

1. The patient and her husband be treated as intelligent individuals, guests of the hospital, deserving every consideration and human kindness.
2. Graduate nursing skills be fully utilized:
   a. To indoctrinate and supervise practical nurses and aides in obstetric nursing procedures.
   b. To teach mothers self-care.
   c. To teach parents baby care.
3. Standard postpartum procedures and medications be agreed upon by the obstetric staff.
4. All personnel be thoroughly indoctrinated in the philosophy and procedures of the obstetric department.

Reviews and Abstracts

EDITED BY LOUIS M. HELLMAN, M.D.

REVIEWS OF NEW BOOKS

Abnormal Labor. By L. A. Calkins. 70 pages. Springfield, Ill., 1958, Charles C Thomas, Publisher. $2.75.

In Part I, the first stage of labor is discussed and the author describes the characteristic pattern of uterine activity. Prolonged labor, uterine inertia, and precipitous labor are aberrations of the basic pattern. Labor in the elderly primigravid patient is the same as in her younger counterpart but a cesarean section is indicated when associated abnormal presentations or a large baby is present. Amniotomy for the induction of labor presents the hazard of intra-amnionic infection, prolapse of the cord, malpresentation, and unsuspected prematurity. The author is opposed to elective induction of labor for convenience or postmaturity.

In Part II, the abnormalities of the second stage of labor are described. Calkins suggests that although occiput posterior is not an abnormal presentation it should be delivered unrotated unless the rotation tends to occur spontaneously. In a patient in premature labor with a breech presentation, cesarean section is contemplated because of the disproportionate size of the fetal head and incomplete dilatation of the cervix. Undue delay in descent of the term breech leads to the selection of cesarean section for delivery. In the author's experience with brow presentation, the fetal head either extends to a face presentation or flexes to an occiput when there is no obstetrical interference. The dangers and risks of multiple pregnancy, pregnancy in the diabetic patient, hydramnios, and possible complications of the premature spontaneous rupture of the membranes are discussed.

In the third part good rules for the management of the third stage of labor are listed.

The final section is a prediction of the duration of the second stage of labor by an evaluation of the type and number of uterine contractions.

The purpose of this monograph, as expressed by the author, is to present succinctly various problems encountered in parturition. He accomplishes his mission successfully. Since brevity is an objective, several aspects are treated in a paragraph. One cannot expect to agree with all the tenets of his obstetrical philosophy.

Die Toxoplasmose. By O. Thalhammer. 307 pages, with 42 illustrations and 34 tables. Vienna, 1957, Verlag für medizinische Wissenschaften Wilhelm Maudrich. $13.75.

Dr. Thalhammer, in his splendid monograph, covers the entire subject of toxoplasmosis, beginning with its history, running through bacteriological tests, and, finally, giving a full discussion of congenital and acquired toxoplasmosis, toxoplasmosis in animals, and the treatment of disease.

Of special interest to obstetricians are the sections on congenital toxoplasmosis. There is a full discussion of toxoplasmosis in the form of acute encephalitis, in the form

of congenital brain damage, and in its relatively asymptomatic form. There is also a discussion of the transmission of toxoplasma through the placenta and through mother's milk.

Altogether, this is a very fine little book, well illustrated, with an excellent bibliography. It deserves to be translated into English for even wider circulation.

Allergy in Pediatric Practice. By William B. Sherman and Walter R. Kessler. 296 pages, illustrated. St. Louis, 1957, The C. V. Mosby Company. $9.25.

This is a textbook and a manual for the practitioner who does not specialize in allergy. It is briefly, intelligently, and clearly written. Theory is presented as it is needed to elucidate the rationale for treatment regimes and diagnostic methods. Controversial subjects are so labeled, and enough evidence is presented so the reader can weigh it.

For those who wish to be guided further into the subject, there is a well-selected, though rather small, bibliography at the end of each chapter.

The authors have worked under Dr. Robert A. Cooke, and are of the faculty of Columbia University's College of Physicians and Surgeons.

Précis d'obstétrique. By Robert Merger, Jean Lévy, and Jean Melchior. 848 pages, 394 figures. Paris, 1957, Masson & Cie. 6,000 fr.

This obstetrical text is primarily designed for use by the medical student. Its major merits are the thorough organization and the wide range of its subject. It is presented in the form of a well-developed outline. The writing is clear and concise. The figures are abundant, well placed, and well drawn. The content is up to date on new methods of treatment. The last two chapters, one of which is on the newborn, the other on the socio-legal aspects of the field, are worthy inclusions.

There are marked differences with the obstetricians in this country on accepted methods of dealing with particular problems. There is no bibliography; no reference is made to the investigative work of individuals in any particular phase of the field, and no sense of the historical development is imparted.

The divergences in controversial concepts and treatments are usually presented with an indication of the personal convictions of the authors.

BOOKS RECEIVED

Anomalías morfológicas de la placenta y su significado clínico. By Oscar Aguero. 107 pages, 27 illustrations. Caracas, Venezuela, 1957.

Endocrine Aspects of Breast Cancer. Proceedings of Conference held at the University of Glasgow, July 8 to 10, 1957. Edited by Alastair R. Currie. 340 pages, 108 figures, 99 tables. Baltimore, 1958, Williams & Wilkins Company. $8.50.

Endocrine Pathology of the Ovary. By John McLean Morris and Robert E. Scully. 151 pages with 75 illustrations and 7 tables. St. Louis, 1958, The C. V. Mosby Company. $8.50.

How to Write Scientific and Technical Papers. By Sam F. Trelease. 185 pages with 6 figures and 8 tables. Baltimore, 1958, Williams & Wilkins Company. $3.25.

An International Symposium on Aldosterone. By Alex F. Muller and Cecilia M. O'Connor. 232 pages, 84 illustrations. Boston, 1958, Little, Brown & Company. $8.00.

Neomycin—Its Nature and Practical Application. Edited by Selman A. Waksman. 412 pages with 41 figures and 93 tables. Baltimore, 1958, Williams & Wilkins Company. $5.00.

Recent Advances in Obstetrics and Gynecology. By Aleck W. Bourne and Leslie H. Williams. Ninth edition. 348 pages with 78 illustrations and 9 tables. Boston, 1958, Little, Brown & Company. $8.00.

SELECTED ABSTRACTS*

The Lancet

Vol. 1, January 4, 1958.

*Goodwin, J. F.: Pregnancy and Coarctation of the Aorta, p. 16.

*Schwarz, V., Holzel, A., and Komrower, G. M.: Laboratory Diagnosis of Congenital Galactosemia at Birth, p. 24.

Goodwin: Pregnancy and Coarctation of the Aorta, p. 16.

To the 123 instances of concurrent coarctation of the aorta and pregnancy which have been described in the medical literature, the author adds 13 others, including 10 which have been reported previously (Cleland et al.: Brit. M. J. 2: 379, 1956). These 136 patients had 354 pregnancies. In all, 13 women died, 8 of whom had associated cardiac defects in addition to the coarctation. The mortality rate connected with pregnancy was therefore 9.5 per cent, but, that related to total pregnancies was 3.4 per cent. The deaths were due to rupture of the aorta (3), rupture of dissecting aneurysm (3), cerebral vascular accident (2), infective endocarditis of aortic valve (1), unknown cause (1), congestive heart failure (2), and pulmonary edema (1). In the author's personal cases there were no deaths despite the fact that all but one of the women had more than one pregnancy. In 10 of the 13 women, the coarctation was resected and there were 2 successful pregnancies subsequently. As others have reported (Dixon and Hartley: J. Obst. & Gynaec. Brit. Emp. 62: 83, 1955; Pritchard: Obst. & Gynec. Surv. 8: 775, 1953), the author found that the pregnancy had no effect upon the associated hypertension.

While surgical correction of the coarctation should undoubtedly be undertaken early in life, the author doubts that the hazards of uncomplicated coarctation are increased by pregnancy. When serious cardiac disease is also present, the hazards are greater. The second pregnancy of one of the author's patients had to be terminated because of aortic incompetence.

DAVID M. KYDD

Schwarz, Holzel, and Komrower: Laboratory Diagnosis of Congenital Galactosemia at Birth, p. 24.

Inasmuch as a galactose-tolerance test may be not without danger to an infant, a laboratory test was developed to establish the diagnosis without administering galactose to the infant. The test may be used whenever the family history suggests the possibility of galactosemia.

The erythrocytes from cord blood are incubated with galactose and then with glucose. After washing with saline, the inorganic and organic phosphates are precipitated with barium and the galactose and glucose-1-phosphates are hydrolyzed and separated chromatographically. Whereas in normal blood between 0.7 and 9.8 γ galactose per milliliter of red cells is found, in 2 instances of galactosemia more than 50 γ galactose per milliliter of red cells was found.

By this method the diagnosis was made at birth in a third infant even though no galactose was detected in the mother's venous blood on 2 occasions after she drank a pint of milk.

DAVID M. KYDD

*Titles preceded by an asterisk are abstracted below.

Vol 1, January 18, 1958.

*Browne, F. J.: Etiology of Pre-eclamptic Toxaemia and Eclampsia, p. 115.

*Bayless, R. I. S., Marrack, D., Pirkis, J., Rees, J. R., and Zilva, J. F.: Chlorothiazide: an Oral Diuretic, p. 120.

Browne: Etiology of Pre-eclamptic Toxaemia and Eclampsia, p. 115.

In a paper read at a joint meeting of the Colloquia on Hypertension and Pregnancy Toxaemia and the Fourth Conference in Australia of the Royal College of Obstetricians and Gyaecologists held in Sydney, August 28, 1957, the author attempted to explain 8 facts peculiar to eclampsia that have hitherto prevented the establishment of a satisfactory etiology of eclampsia: (1) why it occurs only in association with pregnancy and only in man; (2) its preference for first pregnancies (75 per cent of cases); (3) why it sometimes occurs in pregnancy with hydatidiform mole and no fetus, and that very early in pregnancy; (4) why it is five or six times as common in twin as in single pregnancies; (5) why it occurs in 50 per cent of pregnancies with chronic hypertension; (6) its greater frequency in diabetic pregnant patients; (7) why it is often associated with "red infarcts" of the placenta, or with concealed accidental hemorrhage, or with renal cortical necrosis; and (8) why it often occurs two or three days after delivery (10 per cent of cases).

The most important role in the exegesis was assigned to the production of hormones that occurs in pregnancy. Not only is the anterior lobe of the pituitary stimulated to produce an increased secretion of corticotrophin but the latter is produced by the placenta as well. Increased levels of corticosteroids have been found in the sera of pregnant women as often, in fact, as have been found in Cushing's syndrome, leading J. S. L. Browne to speak of normal pregnancy as "a kind of physiological Cushing's syndrome." The concentration of the corticosteroids in the serum increases during pregnancy, further increases immediately after delivery, and returns to normal within a week.

Following the lead of Luschinsky and Singher (Arch. Biochem. 19: 95, 1948) and Thompson and Tickner (Biochem. J. 45: 125, 1949) that there is in the placenta a monoamine oxidase capable of inactivating vasoconstrictor amines, the proposal was made that this is the reason hypertension does not occur in normal pregnancy despite the increased concentration of corticosteroids found. In furtherance of this hypothesis, the author has found that following delivery, when the concentration of corticosteroids is still high and the placenta is absent, 25 to 30 per cent of normal women do develop a transient hypertension.

Studies (Browne and Veall, J. Obst. & Gynaec. Brit. Emp. 60: 141, 1953) have shown that the blood flow in the placenta is reduced to about one half in pre-eclamptic and in chronically hypertensive women. In twin pregnancy the blood supply to the wall is reduced (Morris, Osborn, and Wright, Lancet 1: 323, 1955) possibly by overdistention. Overdistention, or the possibility suggested by Beker (J. Obst. & Gynaec. Brit. Emp. 55: 756, 1948) that the uterus in young primigravidas may have a hypoplastic vascular system, might lead to decreased blood flow and an inefficient placenta so far as the production of the necessary oxidase is concerned, if hypertension is to be prevented. Hypertension, uteroplacental apoplexy, renal cortical necrosis all are associated with arterial spasm. The chorionic villi in hydatidiform moles may secrete corticotrophin and, if so, the occurrence of eclampsia early in the course might be explained. The occurrence of eclampsia after delivery may be caused by the withdrawal of whatever protection the defective placenta may have provided. The frequency of toxemia in diabetic patients could not be explained unless there is an associated vascular disease in diabetes.

Finally, the excess of chorionic gonadotrophin present in pre-eclampsia can be explained by its non-destruction and there is evidence that it causes hypersensitivity of the vascular system known to occur in pre-eclamptic toxemia.

Pre-eclamptic toxemia and eclampsia may be due to the increase in corticosteroids found in normal pregnancy that are not destroyed in the placenta as they normally are because of circulatory abnormalities or a deficient placenta.

DAVID M. KYDD

Bayless et al.: Chlorothiazide: an Oral Diuretic, p. 120.

Twenty-four patients, of whom 17 had congestive heart failure, 3 premenstrual edema, and 4 edema of other causes (cirrhosis, nephrosis, malignant obstruction), were given 1 Gm. of chlorothiazide twice a day. Good results (clearing of edema) were obtained in 14 patients, less satisfactory in 7, and poor in 3. In all but the 3 instances of premenstrual edema the salt intake was restricted. A loss of potassium was the only important electrolyte abnormality noted. Although the results were given as good in the 3 patients with premenstrual edema, the change in weight is recorded in only one; 4 pounds was lost on one occasion and 5 on another. The weight was promptly replaced as soon as the drug was discontinued in this condition.

DAVID M. KYDD

Vol. 1, January 25, 1958.

*Robinson, M.: Salt in Pregnancy, p. 178.

Robinson: Salt in Pregnancy, p. 178.

Alternate patients, on their first prepartal visits, were put into groups S and S–. Those in group S were advised to increase their salt intake, while those in group S– were told to restrict their salt intake throughout pregnancy. There were 1,019 patients in group S and 1,000 in group S–. The two groups were comparable in regard to distribution by age, parity, and weeks of gestation when first seen. The incidence of toxemia was 3.8 per cent in the group on high salt intake and 9.7 per cent in the group told to restrict salt. In primigravidas, the incidence of toxemia was 11.1 per cent and 26.1 per cent, respectively. The incidence of edema, perinatal death, antepartum hemorrhage, and bleeding in pregnancy was also lower in the group on high salt intake.

Twenty patients who developed toxemia were advised to take extra salt, as the only treatment. The signs and symptoms of toxemia disappeared in 17; the larger the salt supplement, the quicker and more complete was the recovery. When extra salt was not taken until delivery, the toxemia recurred. (Comment: It would not be astonishing if about the same incidence of toxemia had been found in the 2 groups, but it is hard to understand why one of every 4 primigravidas should develop toxemia in the group told to restrict salt intake. Of course, no amount of theorizing can offset factual observation, but the "cure" of toxemia by high salt intake is contrary to the experience of all who have given intravenous salt to toxemic patients. In Dieckmann's salt test, one of the criteria for diagnosing pre-eclampsia is the worsening of the signs and symptoms when sodium chloride is given intravenously. One would not expect opposite effects from oral and parenteral salt administration.)

LEON C. CHESLEY

Vol. 1, February 1, 1958.

*Smyth, C. N.: Uterine Irritability. The Concept and Its Clinical Applications, Exemplified by the Oxytocin-Sensitivity Test, p. 237.

*Ashley, D. J. B., and Jones, C. H.: Discrepancies in the Diagnosis of Genetic Sex by Leucocyte Morphology, p. 240.

Smyth: Uterine Irritability. The Concept and Its Clinical Applications, Exemplified by the Oxytocin-Sensitivity Test, p. 237.

By the intravenous administration of minimal doses of oxytocin (0.01 to 0.1 unit), the amount required to produce a measurable increase in uterine activity was found to correlate with the imminence of labor even though there is no correlation with the length of labor.

Sensitivity to 0.02 unit or less of oxytocin indicated that labor would begin spontaneously within a few hours. A sensitivity to between 0.02 and 0.04 unit usually indicated that labor would start within 1 to 3 days although there was considerable scattering when the higher values were involved. Perhaps the two best uses of the test are: (1) to help to determine whether labor is more or less imminent by repetitive tests on succeeding days; and (2) in instances where labor is to be induced, to predict the success of amniotomy. When the oxytocin test has a numerical value of 0.04 unit or less amniotomy is very successful and is progressively less so as the sensitivity approaches 0.08 unit.

DAVID M. KYDD

Ashley and Jones: Discrepancies in the Diagnosis of Genetic Sex by Leucocyte Morphology, p. 240.

Two techniques have been developed for the diagnosis of genetic sex: (1) an examination of the intermitotic cells of the skin and many other tissues (Moore and Barr: Acta anat. 21: 197, 1954); (2) an examination of the nuclei of the polymorphonuclear cells (Davidson and Smith; Brit. M. J. 2: 6, 1954). In this report two instances are detailed in which there was a discrepancy found between the two techniques.

In the first, a child of 20 months who was considered to be an example of complete sex reversal in that the nuclear sex is male but the phenotype female, cells from the skin and buccal mucosa always showed heterochromatin in less than 6 per cent of the nuclei (male), but examination of the blood film showed that the characteristic "drumsticks" were present in 3 per cent of the polymorphonuclear cells (female).

In the second patient, a child of 14 months with Turner's syndrome, examination of the cells from the buccal membrane showed heterochromatin in 4 per cent of the cells (male) but in the blood smear, 7 per cent of the polymorphonuclear cells showed "drumsticks" (female).

The authors note that such discrepancies have been reported previously. Heretofore, the discrepancy has always been in the same direction, i.e., the nuclear sex was female but the polymorphonuclear cells indicated male. The direction is reversed in the 2 patients in the present report, however. The suggestion is made that, although the examination of the polymorphonuclear cells warrants further investigation, more reliance be placed on the study of the nuclei of other cells such as those from the buccal membrane in determining genetic sex.

DAVID M. KYDD

Vol. 1, February 8, 1958.

*FitzGerald, T. B., and Clift, A. D.: The Fetal Loss in Pregnancy Toxemia, p. 283.

FitzGerald and Clift: The Fetal Loss in Pregnancy Toxemia, p. 283.

In 819 instances of toxemia that occurred during a 5 year period at the Ashton-Under-Kyne General Hospital in Lancastershire, 72 of the pregnancies ended in stillbirth or neonatal death. Of these, 29 fetuses (40 per cent) died in utero before the onset of labor, 19 (26 per cent) died of accidental hemorrhage, 14 (19 per cent) died during delivery, and 10 (14 per cent) died shortly after delivery. In every instance, the birth weights of fetuses who died in utero were less than the normal fetal weight at the same period of gestation, whereas the fetuses who died following an accidental hemorrhage weighed as much as the normal fetuses. The suggestion is made that there are 2 different ways in which fetal death takes place in toxemia of pregnancy. In one group, growth is diminished or ceases and the baby "fades out," presumably because of a lack of adequate oxygen or nutrients. In the other, placental function remains adequate until there is an abrupt stripping of the placenta from its bed by hemorrhage.

Nearly 90 per cent of the deaths caused by accidental hemorrhage and 70 per cent of the intrauterine deaths occurred before the thirty-seventh week of gestation. Consequently, when a fetus is not growing normally, the dangers of prematurity caused by induction before the thirty-seventh week must be weighed against the risk of intrauterine death in the toxemias of pregnancy. The timing of delivery may be of more importance than the method.

DAVID M. KYDD

Quarterly Review of Surgery, Obstetrics and Gynecology

Vol. 14, 1957.

*Goldfarb, W. S.: Contractions of the Human Uterus and a Theory of Labor, p. 142.

Goldfarb: Contractions of the Human Uterus and a Theory of Labor, p. 142.

The response of strips of human myometrium obtained from 5 patients undergoing cesarean section at full term was studied. Carbon dioxide, being passed into a previously oxygenated physiological saline bath in which strips of human myometrium were suspended, produced a tetanic contraction of tissue similar to that which occurs in human labor. It was possible to relax the contracted muscle by stopping the carbon dioxide and increasing the oxygen content of the tissue bath.

It was postulated that, as the uterus grows with its products of gestation, a greater blood and oxygen supply is necessary. The caliber of the larger arteries to the uterus remains unchanged, however. By such growth of the uterus, catabolites accumulate because of the progressive inadequacy of the blood supply and a point is reached at which the carbon dioxide content in the blood of the uterine wall is such that it stimulates the myometrium to contract. It is believed that the uterus initiates labor on this basis.

If the carbon dioxide concentration in the blood vessels of the human uterine muscle is near the critical level, the administration of a vasoconstrictor such as posterior pituitary extract or an epinephrine solution will produce further vasoconstriction that will increase the carbon dioxide content of the uterine muscle and cause contraction of the muscle fibers.

Premature labor can occur because of an overripening of the uterine vascular supply so that the critical carbon dioxide level in the wall of the uterus is reached prematurely. Such premature labors are the result of a deficient blood supply to the uterine muscle.

At the other extreme, uterine inertia could be the result of insufficient ripening of the vascular supply, so that the critical level of carbon dioxide is not present in the uterine wall. Such cases could be and are corrected by administering a vasoconstrictor such as posterior pituitary extract.

JOHN J. DETTLING

Surgery, Gynecology and Obstetrics

Vol. 105, November, 1957.

*Pritchard, Jack A., and Adams, Reuben H.: The Fate of Blood in the Peritoneal Cavity, p. 621.

*Schwartz, Arthur E., and Brunschwig, Alexander: Radical Panhysterectomy and Pelvic Node Excision for Carcinoma of the Corpus Uteri, p. 675.

Pritchard and Adams: The Fate of Blood in the Peritoneal Cavity, p. 621.

This study was undertaken in an attempt to determine whether it is beneficial to leave the blood in the peritoneal cavity at the time of operation in cases of intraperitoneal hemorrhage. To measure the number of red cells transferred from the peritoneal cavity to the intravascular compartment, the authors labeled the intraperitoneal erythrocytes with radioactive chromium in the form of sodium chromate.

The patients studied were divided into three groups. The first was made up of 8 patients with ruptured tubal pregnancies. In these, the liquid blood in the peritoneal

cavity was aspirated, mixed with acid citrate dextrose solution, and then reintroduced into the peritoneal cavity at the time of closure of the peritoneum. The second group was made up of 7 recently postpartum patients who were undergoing bilateral tubal ligation. In this group blood was drawn from the antecubital fossa one to two hours before operation, mixed with acid citrate solution, labeled, and then placed in the peritoneal cavity at the time of operation. The third group consisted of 5 patients undergoing bilateral tubal ligation. In these, blood was placed in the peritoneal cavity directly from a compatible donor at the time of closure of the peritoneum. The donor blood had been previously labeled, but this group differed in that the blood placed in the peritoneal cavity had not been mixed with the acid citrate solution to inhibit clotting.

The authors concluded that:

1. Relatively slight effect on the level of circulating hemoglobin from actual transfer of hemoglobin in erythrocytes from the peritoneal cavity to the intravascular compartment can be anticipated from erythrocyte absorption.

2. Although the volumes of blood placed in the peritoneal cavity frequently were large, the amount of hemoglobin transferred to the subject's total hemoglobin mass was actually quite small.

3. The administration of replacement iron, orally, intravenously, or intramuscularly results usually in hemoglobin production in excess of the amount in erythrocytes transferred to the blood stream during the same period of time.

4. The presence of a large volume of blood in the peritoneal cavity may increase postoperative morbidity.

The authors recommend that in cases of extensive intraperitoneal hemorrhage the blood be removed at the time of operation, and that iron be given to replace the amount lost in the discarded hemoglobin.

VINCENT TRICOMI

Schwartz and Brunschwig: Radical Panhysterectomy and Pelvic Node Excision for Carcinoma of the Corpus Uteri, p. 675.

This is a review of 96 cases of endometrial carcinoma treated by radical panhysterectomy or excision of a cervical stump combined with pelvic node dissection. The surgical and hospital mortality was 2 per cent and the incidence of urinary tract fistulas was 8 per cent. In 13 of the 96 patients metastatic cancer was found in the pelvic lymph nodes, an incidence of 14 per cent. Of these 13 cases, in 7 the metastases involved the hypogastric nodes and in 5 the parametrial nodes also contained metastasis. Two of the 13 patients who had metastasis of the pelvic nodes are living and well more than 5 years following the surgical procedure, while the survival rate of 37 patients followed 5 or more years is 73 per cent.

The authors feel that a poor prognosis is related to the depth of myometrial invasion rather than to the primary location of the lesion within the uterus. Involvement of the isthmus or endocervix from a primary lesion in the fundus is a bad prognostic sign because of its association with deep myometrial invasion, pelvic node involvement, and distant metastasis rather than its location per se. From this study, it appears that lesions arising in the isthmus have a prognosis no worse than those arising in the fundus when myometrial invasion is not present.

It is the authors' opinion that radical panhysterectomy with pelvic node excision, the status of the patient permitting, is the procedure of choice for corporeal carcinoma because if metastases are present in the nodes the patient will be given the benefit of their excision. Further, in the absence of involved lymph nodes this operation is preferable to simple panhysterectomy on the basis of the principle that wide excision should be performed for a malignant lesion.

VINCENT TRICOMI

Wiener klinische Wochenschrift

Vol. 69, October 4, 1957.

*Grasberger, A., and Zeiss, R.: Observations on Puerperal Mastitis and Its Treatment With X-ray, p. 776.

Grasberger and Zeiss: Observations on Puerperal Mastitis and Its Treatment With X-ray, p. 776.

The authors point out that the treatment of puerperal mastitis was extremely efficient during the first years of the penicillin era, but that this preliminary result was followed by a definite diminution of effectiveness as organisms became penicillin fast. The authors have observed an increased incidence of puerperal mastitis during the last several years. They believe that, in addition to the penicillin fastness of the organisms, the change in environment from home to hospital promotes the inception of the infection in small superficial lesions of the nipple.

The total incidence of mastitis in 2,797 deliveries was 213, or 7.6 per cent. In addition to the usual treatments of breast binding, hot moist packs, and antibiotic injections, the authors have started to use x-irradiation as a part of the routine treatment. They give the specific data for their method, which involves a surface dose of some 10 r, over a total field measuring 6 by 6 cm. This is undertaken once a day until symptoms subside. There was no apparent diminution in the amount of milk produced by the breast during the irradiation period. The prognosis was very much better in the patients in whom this treatment was begun soon after the signs of inflammation appeared, rather than in the late cases first treated after 12 days. The authors recommend their method for the treatment of puerperal mastitis when it is diagnosed in its early stage, and point out its cosmetic advantages.

DOUGLAS M. HAYNES

Item

American Board of Obstetrics and Gynecology

Applications for certification (American Board of Obstetrics and Gynecology), new and reopened, Part I, and requests for re-examination Part II, are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of application is Sept. 1, 1958. No applications can be accepted after that date.

Candidates for admission to the Examinations are required to submit with their application an unbound 8½ by 11 inch typewritten list of all patients admitted to the hospitals where they practice, for the year preceding their application, or the year prior to their request for reopening of their application.

Current Bulletins outlining present requirements may be obtained by writing to the Secretary's office.

ROBERT L. FAULKNER, M.D., SECRETARY
2105 ADELBERT ROAD
CLEVELAND 6, OHIO

Correspondence

Toxemia and Placenta Previa, Coexistence and Symptomatology

To the Editors:

In the February, 1958, issue of the JOURNAL there is a remarkable report by Dr. Bieniarz on the lack of coexistence of toxemia of pregnancy and placenta previa.

Using Dr. Bieniarz's data we find an incidence in 25,000 cases of pregnancy of some 3.8 cases per thousand of toxemia and some 2.7 cases per thousand of placenta previa. The expected chance coincidence of these conditions would be a rare 10.4 per million or 1 per 100,000 pregnancies, a series 4 times the size of the author's.

Thinking of the relative frequency of total and incomplete placenta previa, and the fact that few obstetricians routinely explore the uterine cavity prior to separation of the placenta, I suspect we might indeed find more marginal previas in patients with toxemia, thus fulfilling the difference in placental sites which Dr. Bieniarz considers as significant in the causation of toxemia of pregnancy. I should judge that in a series of 25,000 cases the lack of a patient with both conditions is not in the least unusual.

D. R. SHANKLIN, M.D.
INSTRUCTOR IN PATHOLOGY

BOX 3216
DURHAM, NORTH CAROLINA
FEBRUARY 7, 1958

Reply by Dr. Bieniarz

To the Editors:

I highly appreciate the interest shown by Dr. Shanklin in my report as well as his sound criticism. His remarks as to the insufficiency of my material to make a conclusive statement about the lack of coexistence of placenta previa and eclampsia are entirely correct.

Nevertheless, I cannot get rid of the impression that, concentrating on this purely marginal detail, Dr. Shanklin has missed the main point of the article. As the title shows, it deals with a *marked contrast in clinical symptomatology between toxemia and placenta previa,* and not with the lack of coexistence between these two complications. Dr. Shanklin knows quite well, as I know, that even quadrupling my material to 100,000 pregnancies without finding the expected 1 case of coexistence of placenta previa and eclampsia would be a very poor proof of lack of such coexistence. Only by going through several hundred thousands or even millions of observations might more reassurance be reached on this point, which did not seem important enough, especially in view of the far more interesting difference in clinical symptomatology between those two complications. Backed by the statements of some of the most experienced obstetricians with whom I was in touch, I only stated that the association seems very rare, indeed.

The difference in clinical symptomatology between placenta previa and toxemia, which was my main topic, proved statistically highly significant, even with my limited clinical material of 25,000 pregnancies. Such definite contrast in clinical symptomatology as was found is very unlikely to be due to chance and there must be an essential cause for it. The search for this cause seemed far more interesting and promising than the lack of coexistence of placenta previa and eclampsia, because it might possibly be correlated with the cause of toxemia and hemorrhage itself.

J. Bieniarz, M.D.
Medical Academy, Gdańsk
Associate in Obstetrics and Gynecology
First Woman's Clinic, Gdańsk, Poland

Present address:
Department of Anatomy
University of Illinois College of Medicine
1853 West Polk Street
Chicago 12, Illinois
March 17, 1958

Credit for Earlier Statements on Endometriosis and Pseudopregnancy

To the Editors:

Re: Kistner, R. W.: The Use of Newer Progestins in the Treatment of Endometriosis, Am. J. Obst. & Gynec. 75: 264, 1958.

I am distressed to note the late date (1953) given to the ideas pioneered by Joe Vincent Meigs. An editorial by Meigs, "Endometriosis—A Possible Etiological Factor" (Surg., Gynec. & Obst. 67: 253, 1938) established ideas that, when used as a therapeutic foundation for the conservative management of endometriosis, have more than proved their validity in the past twenty years.

The statements credited to Joe Vincent Meigs by Kistner as having been made in 1953, were made earlier while he was moderating a round table at the A. M. A. meeting in June, 1948. These remarks appear in the J. A. M. A. 139: 976, 1949. I point this out now since it becomes increasingly apparent that Meigs was way ahead in his thinking, while many gynecologists have been far behind in their reading.

Dr. Kistner further writes of inducing amenorrhea (pseudopregnancy) without giving credit to *another pioneer*, K. J. Karnaky, for originally producing a substitute pregnancy (Use of Stilbesterol for Endometriosis, South M. J. 41: 1109, 1948). I suggest that we face the fact that obstetrics and gynecology is not a new specialty. It has a very long heritage of able men and we today could at least honor them by reading what they wrote.

Clayton T. Beecham, M.D.

155 West Walnut Lane
Philadelphia 44, Pennsylvania
February 10, 1958

Reply by Dr. Kistner

To the Editors:

I wish to thank Dr. Beecham for noting the earlier publications of Dr. Meigs. In view of the fact that the idea of "pseudopregnancy" suggested itself following the admonitions of Dr. Meigs, I submitted my manuscript to him for review before publication. Since the paper in question was not a review article it was not deemed advisable to list all of the previous articles Meigs had published in this particular regard.

I do not regard the state resulting from use of diethylstilbestrol alone as a "pseudopregnancy." The latter term has been used by many authors (Bradbury, J. J.; Brown, W.;

Rock, J.; Horne, H. W.) to indicate a state induced by the simultaneous, prolonged use of estrogen and progesterone.

ROBERT W. KISTNER, M.D.

FREE HOSPITAL FOR WOMEN
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BROOKLINE 46, MASSACHUSETTS
APRIL 28, 1958

Perinatal Mortality Statistics

To the Editors:

We have read with interest Dr. Orvan H. Hess' paper, "Factors Influencing Perinatal Mortality in Cesarean Section," appearing in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY 75: 376, February, 1958.

Dr. Hess has correctly stated that in New York City (page 377), "a 19.5 per cent decrease in the perinatal mortality rate occurred during the years 1946 to 1953, with a decline of 12.0 per cent in early neonatal deaths (i.e., under 1 week of age)." These statistics were published by one of us (E. M. G.) as Table 1 in a paper, "Perinatal Mortality," J. A. M. A. 159: 244, September 24, 1955. We presume through oversight Dr. Hess failed to give bibliographic reference thereto.

Dr. Hess further states (page 377), "In 1953, the perinatal mortality rate in New York City was reported to have been 29.7 per 1,000, while in 1955 it had decreased to 20 per 1,000 births." We in New York City would be very proud to acknowledge such a sharp decline in a 2 year period. As a matter of fact, however, the perinatal mortality rate for New York City for the year 1955 was 30.4. The rate in 1956 was 28.9.

We are hoping that, within the not too distant future, our educational efforts will be rewarded by a reduction of the present perinatal mortality to the salutary rate of 20, prematurely credited to us.

EDWIN M. GOLD, M.D.
HAROLD JACOBZINER, M.D.
ASSISTANT COMMISSIONER
MATERNAL AND CHILD HEALTH SERVICES
NEW YORK CITY DEPARTMENT OF HEALTH
JEAN PAKTER, M.D.
CHIEF, MATERNITY AND NEWBORN DIVISION
NEW YORK CITY DEPARTMENT OF HEALTH

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BROOKLYN 17, NEW YORK (DR. GOLD)
FEBRUARY 18, 1958

Reply by Dr. Hess

To the Editors:

The statistics in the letter of Drs. E. M. Gold, H. Jacobziner, and J. Pakter which are quoted in paragraph 2 and in the portion of paragraph 3, "In 1953, the perinatal mortality rate in New York City was reported to have been 29.7 per 1,000," were published by Edwin M. Gold, M.D., in a paper entitled "Perinatal Mortality," J. A. M. A. 159: 244, Sept. 24, 1955. I sincerely regret that, through oversight, reference to his important contribution on this subject failed to appear in the bibliography of my paper, "Factors Influencing Perinatal Mortality in Cesarean Section," AM. J. OBST. & GYNEC. 75: 376, February, 1955.

The statement in my paper that "in 1955 it had decreased to 20 per 1,000 births" was an error in typing of an early revision of the manuscript. The information, submitted in the letter of Drs. Gold, Jacobziner, and Pakter, that the perinatal mortality rate in New York City was 30.4 per 1,000 for 1955 indicates that, in comparison with 29.7 per 1,000 for 1953, a decrease in perinatal mortality rate in New York City did not occur during that 2 year period.

ORVAN W. HESS, M.D.

79 TRUMBULL STREET
NEW HAVEN, CONNECTICUT
MARCH 27, 1958

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January and July)

American College of Obstetricians and Gynecologists. (1951) *President,* R. Glenn Craig. *Secretary,* John C. Ullery, Starling-Loving Bldg., The Ohio State University, Columbus, Ohio. Next meeting, Atlantic City, N. J., April 6, 7, and 8, 1959.

American Gynecological Society. (1876) *President,* Howard C. Taylor, Jr., New York, N. Y. *Secretary,* Andrew A. Marchetti, Georgetown University Hospital, Washington 7, D. C. Annual meeting, May, 21, 22, and 23, 1959.

American Association of Obstetricians and Gynecologists. (1888) *President,* William F. Mengert, Chicago, Ill. *Secretary,* E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Colo. Annual meeting, Sept. 4-6, 1958.

Central Association of Obstetricians and Gynecologists. (1929) *President,* Herbert E. Schmitz, Chicago, Ill. *Secretary,* Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Ill. Annual meeting, Hotel Leamington, Minneapolis, Minn., Oct. 2-4, 1958.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President,* Charles J. Collins. *Secretary,* W. Norman Thornton, Jr., University of Virginia Hospital, Charlottesville, Va. Next meeting, Roanoke, Va., Feb. 4-7, 1959.

A. M. A. Section on Obstetrics and Gynecology. (1859) *Chairman,* Woodard D. Beacham, New Orleans, La. *Secretary,* Keith P. Russell, 511 S. Bonnie Brae St., Los Angeles 57, Calif. Next meeting, Atlantic City, N. J., June 8-12, 1959 (Centennial Meeting of Section).

Society of Obstetricians and Gynaecologists of Canada. (1944) *President,* J. S. Henry, Montreal, Quebec. *Secretary,* F. P. McInnis, 280 Bloor St. W., Toronto 5, Ont. Annual meeting, Mont Tremblant Lodge, Mont Tremblant, Quebec, Sept, 10-13, 1959.

American Board of Obstetrics and Gynecology, Inc. (1930) *President,* Bayard Carter. *Secretary,* Robert L. Faulkner, 2105 Adelbert Rd., Cleveland 6, Ohio.

Akron Obstetrical and Gynecological Society. (1946) *President,* B. N. Riddle. *Secretary,* Louis M. Walker, 1108 Second National Bldg., Akron 8, Ohio. Meetings, quarterly.

Alabama Association of Obstetricians and Gynecologists. (1940) *President,* Julian P. Hardy. *Secretary,* Lyman Findley, 819 Fourth Ave., Tuscaloosa, Ala. Next meeting, Birmingham, Ala., April 15, 1959.

Alameda-Contra Costa Gynecological Society. (1951) *President,* Wallace Lawson. *Secretary,* Clifford Chappell, 2636 Telegraph Ave., Berkeley, Calif. Meetings, fourth Wednesday, September to June.

Arkansas Obstetrical and Gynecological Society. (1953) *President,* J. F. Kelsey. *Secretary,* Arthur F. Hoge, 1600 Rogers Ave., Fort Smith, Ark. Meetings, May and October.

Atlanta Obstetrical and Gynecological Society. (1954) *President,* George A. Williams. *Secretary,* William H. Grimes, Jr., 272 Boulevard, N. E., Atlanta 12, Ga. Meetings, February, April, June, and October.

Birmingham Obstetrical and Gynecological Society. (1949) *President,* Ernest B. Oliver. *Secretary,* Eugene Howe, 920 S. 19th St., Birmingham 5, Ala. Meetings, last Thursday in January and March.

Boston, Obstetrical Society of. (1861) *President,* Alfred L. Potter. *Secretary,* A. Gordon Gauld, 1180 Beacon St., Brookline 46, Mass. Meetings, third Monday, January, February, March, April, October, and November.

Bronx Gynecological and Obstetrical Society. (1924) *President,* Bernard Lapan. *Secretary,* Sidney S. Steckel, 800 Grand Concourse, Bronx 51, N. Y. Meetings, fourth Monday, October, November, January, February, March, and April.

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*Changes, omissions, and corrections must be received by the publisher two months in advance, by May 1 for the July Roster and by November 1 for the January Roster. Please address The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. The number after the Society's name is the year of founding. For further information, address the respective secretaries.

Brooklyn Gynecological Society, Inc. (1890) *President,* Arthur T. Antony. *Secretary,* Warren A. Lapp, 731 E. 22nd St., Brooklyn 10, N. Y. Meetings, third Wednesday, October, November, January, February, March, April, and May.

Buffalo Obstetrical and Gynecological Society. (1946) *President,* Milton H. Kahn. *Secretary,* Chester Kaminski, 333 Linwood Ave., Buffalo 9, N. Y. Meetings, October through May.

Central New York Association of Gynecologists and Obstetricians. (1938) *President,* Eugene R. Duggan. *Secretary,* James N. Capps, 325 University Ave., Syracuse, N. Y. Meetings, second Tuesday of September, November, January, March, and May.

Chicago Gynecological Society. (1878) *President,* H. Close Hesseltine. *Secretary,* William G. Cummings, 636 Church St., Evanston, Ill. Meetings, third Friday, October through June.

Cincinnati Obstetrical and Gynecological Society. (1876) *President,* Lester J. Bossert. *Secretary,* John M. Glenn, 3180 Harrison Ave., Cincinnati, Ohio. Meetings, third Thursday, September through June.

Cleveland Society of Obstetrics and Gynecology. (1947) *President,* Edwin D. Richards. *Secretary,* Richard Glove, 3550 Warrensville Center Rd., Shaker Heights 22, Ohio. Meetings, fourth Monday, September, November, January, March, and May.

Columbus Obstetric-Gynecologic Society. (1944) *President,* Fred Hapke. *Secretary,* Harry E. Ezell, Jr., 81 S. Fifth St., Columbus, Ohio. Meetings, last Wednesday of month, September through May, except December.

Connecticut Society of American Board Obstetricians and Gynecologists, Inc. (1952) *President,* Hugh K. Miller. *Secretary,* Joseph Klein, 435 Farmington Ave., Hartford 5, Conn. Meetings. April and October.

Dallas-Fort Worth Obstetric and Gynecologic Society. (1948) *President,* Herman I. Kantor. *Secretary,* James T. Downs, III, 3707 Gaston Ave., Dallas 10, Texas. Meetings, spring and fall.

Dayton Obstetrical and Gynecological Society. (1937) *President,* H. E. McKnight. *Secretary,* Paul G. Seyler, Fidelity Medical Bldg., Dayton 2, Ohio. Meetings, third Wednesday each month.

Denver Gynecological and Obstetrical Society. (1942) *President,* Gerard Del Junco. *Secretary,* Alvin J. Frosh, 2222 East 18th Ave., Denver, Colo. Meetings, first Monday of every month, October through May, inclusive.

Florida Obstetric and Gynecologic Society. (1948) *President,* J. W. Douglas. *Secretary,* T. Bert Fletcher, Jr., 1203 Miccosukee Rd., Tallahassee, Fla. Meetings, Dec. 6-7, 1958, and spring, 1959.

Georgia State Obstetrical and Gynecological Society. (1951) *President,* Charles Mulherin, Augusta, Ga. *Secretary,* Bothwell Traylor, 419 S. Milledge Ave., Athens, Ga. Meetings, spring and fall.

Harris, John Warton, Obstetrical Society. (1953) *President,* William V. Luetke. *Secretary,* Madeline J. Thornton, University Hospitals, Madison, Wis. Annual meeting, first week in June.

Honolulu Obstetrical and Gynecological Society. (1947) *President,* Fugate Carty. *Secretary,* John Ohtani, Rm. 410, Professional Center Bldg., Honolulu, Hawaii. Meetings, third Monday of each month.

Houston Gynecological and Obstetrical Society. *President,* J. P. Salerno. *Secretary,* William R. Knight, III, 724 Hermann Professional Bldg., Houston 25, Texas. Meetings by announcement.

Indiana Obstetrical and Gynecological Society. (1947) *President,* Mahlon Miller. *Secretary,* John E. Mackey, 3400 N. Meridian St., Indianapolis, Ind. Meetings, second Wednesday, October, January, and April.

Interurban Obstetrical and Gynecological Society. (1949) *President,* Arthur J. Wallingford, Albany, N. Y. *Secretary,* E. R. Duggan, 16 N. Goodman St., Rochester 7, N. Y. Meeting, October, 1959.

Iowa Obstetrical and Gynecological Society. *President,* Addison Brown. *Secretary,* W. B. Goddard, University Hospitals, Iowa City, Iowa. Meetings, April and November.

Kansas City Gynecological Society. (1922) *President,* Floyd C. Atwell. *Secretary,* Kenneth S. Nicolay, 4635 Wyandotte St., Kansas City 12, Mo. Meetings, September, November, January, March, and May.

Kentucky Obstetrical and Gynecological Society. (1947) *President,* Joseph Liebman, Frankfort, Ky. *Secretary,* Ed. Masters, 107 Fairmeade Rd., Louisville, Ky. Annual meeting in April.

Long Beach Obstetrical and Gynecological Society. (1954) *President,* Mary B. Callaghan. *Secretary,* Philip B. Hartley, 2491 Pacific Ave., Long Beach, Calif. Meetings, quarterly.

Los Angeles Obstetrical and Gynecological Society. (1914) *President,* Alphonsus M. McCarthy. *Secretary,* John L. Gaspar, 16100 Ventura Blvd., Encino and 6753 Hollywood Blvd., Los Angeles 28, Calif. Meetings, second Tuesday, September, November, January, March, and May.

Louisville Obstetrical and Gynecological Society. *President,* Douglas Haines. *Secretary,* Douglas L. Gillim, 501 Heyburn Bldg., Louisville 2, Ky. Meetings, fourth Monday, September, October, November, January, February, March, April and May.

Madison Obstetrical and Gynecological Society. (1950) *President* and *Secretary,* Gerald Kring, 2 W. Gorham St., Madison, Wis. Meetings, first Tuesday each month, September through June.

Maryland, Obstetrical and Gynecological Society of. (1929) *President,* Arthur Hoskins. *Secretary,* Harry M. Beck, 700 N. Charles St., Baltimore 1, Md. Meetings, October, December, February, and May.

Memphis Obstetrical and Gynecological Society. (1950) *President,* Walter A. Ruch. *Secretary,* Robert M. Ruch, Suite 302, 899 Madison Ave., Memphis, Tenn. Meetings, second Tuesday, October through May.

Miami Obstetrical and Gynecological Society. (1946) *President,* William Howdon. *Secretary,* John M. Schultz, 504 Huntington Bldg., Miami 32, Fla. Meetings, second Thursday, January, March, May, and November.

Michigan Society of Obstetricians and Gynecologists. (1924) *President,* James H. Beaton. *Secretary,* Robert G. Swanson, 936 Alter Rd., Detroit 15, Mich. Meetings, first Tuesday, October, December, February, April, and May.

Milwaukee Gynecological Society. (1951) *President,* Carlton Wirthwein. *Secretary,* John Thoma, 411 E. Mason St., Milwaukee 2, Wis. Meetings, fourth Monday, January, March, May, and November.

Minneapolis Obstetrical and Gynecological Society. (1955) *President,* Harold R. Leland. *Secretary,* Richard R. Fliehr, 90 S. 9th St., Minneapolis 2, Minn. Meetings, third Wednesday, September, November, January, and March.

Minnesota Obstetrical and Gynecological Society. *President,* John L. McKelvey. *Secretary,* Edward A. Banner, 200 First St., S. W., Rochester, Minn. Next meeting, Minneapolis, Minn., Nov. 29, 1958.

Mississippi Obstetrical and Gynecological Society. (1947) *President,* J. C. Knox, Jr. *Secretary,* Blanche Lockard, 838 Lakeland Drive, Jackson, Miss. Meetings, May and December.

Mobile County Obstetrical and Gynecological Society. (1949) *President,* O. M. Otts, Jr. *Secretary,* A. K. Conditt, 1367 Government St., Mobile, Ala. Meetings, quarterly when called.

Montgomery County (Ohio) Obstetrical and Gynecological Society. (1937) *President,* L. O. Fredericks. *Secretary,* A. A. Kunnen, 406 Harries Bldg., Dayton, Ohio. Meetings, third Wednesday of each month.

Montana Obstetrical and Gynecological Society. (1946) *President,* Arnold E. Ritt, Great Falls, Mont. *Secretary,* Robert H. Leeds, Chinook, Mont.

Nashville Obstetrical and Gynecological Society. (1955) *President,* Joe Anderson. *Secretary,* James Ellis, Nashville, Tenn. Meetings, March, June, September, and December.

Nassau Obstetrical Society. (1944) *President,* David G. Warden. *Secretary,* A. F. Rowsom, 21 Weir Lane, Locust Valley, N. Y. Meetings, second Monday, October, December, February, and April.

New England Obstetrical and Gynecological Society. (1929) *President,* Alfred L. Potter. *Secretary,* William A. Lynch, 1101 Beacon St., Brookline 46, Mass. Meetings, May and October.

New Haven Obstetrical and Gynecological Society. (1946) *President,* William Richards. *Secretary,* Virginia M. Stuermer, 42 Trumbull St., New Haven 10, Conn. Meetings, third Tuesday, September, November, January, March, and May.

New Jersey Obstetrical and Gynecological Society. (1947) *President,* Henry S. Acken, Jr. *Secretary,* Saul B. Gusberg, 180 Fort Washington Ave., New York 32, N. Y. Meetings, second Tuesday, October through May.

New Mexico Obstetrical and Gynecological Society. (1947) *President,* Robert P. George. *Secretary,* C. H. Rundles, 211 Oak St., N. E., Albuquerque, N. Mex. Meetings, quarterly.

New Orleans Gynecological and Obstetrical Society. (1924) *President,* Abe Mickal. *Secretary,* Julius T. Davis, Jr., 4414 Magnolia St., New Orleans, La. Meetings, October, November, January, March, and May.

New York Obstetrical Society. (1863) *President,* Frank R. Smith. *Secretary,* George L. Bowen, 101 East 74th St., New York 21, N. Y. Meetings, second Tuesday, September through May.

North Carolina Obstetrical and Gynecological Society. (1932) *President,* James F. Donnelly. *Secretary,* James A. Crowell, 412 N. Church St., Charlotte 2, N. C. Next meeting, Mid Pines Club, Southern Pines, N. C., April 24-26, 1959.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* Frank Hill. *Secretary,* G. Wilson Hunter, Fargo Clinic, Fargo, N. D. Meetings, May and September.

Northeastern New York Obstetrical and Gynecological Society. (1935) *President,* Raymond L. Rhodes, Glen Falls, N. Y. *Secretary,* Thomas F. D'Aurio, 17 State St., Troy, N. Y. Meetings, fourth Thursday, January, April, and September.

Northern California Obstetrical and Gynecological Society. (1955) *President,* Marvin G. Sadugor. *Secretary,* Warren E. Jones, c/o Sutter Maternity Hospital, 52nd and F Sts., Sacramento 19, Calif. Meetings, second Friday of March, May, October, and December.

Oklahoma City Obstetrical and Gynecological Society. (1940) *President,* Walter K. Hartford. *Secretary,* William L. Bond, 1200 N. Walker, Oklahoma City, Okla. Meetings, February, April, October, and December.

Omaha Obstetrical and Gynecological Society. (1947) *President,* Robert Collins. *Secretary,* W. H. Taylor, Jr., 3807 Cuming St., Omaha 31, Neb. Meetings, third Wednesday, January, March, May, September, and November.

Oregon Society of Obstetricians and Gynecologists. *President,* Charles Mills. *Secretary,* Keith Markee, 1918 N. W. Johnson St., Portland, Ore. Meetings, third Friday, October through May, except December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President,* Donald J. Thorp, Seattle, Wash. *Secretary,* Donald W. DeCarle, 2000 Van Ness Ave., San Francisco, Calif. Meeting, Olympic Hotel, Seattle, Wash., Oct. 15-18, 1958.

Pacific Northwest Obstetrical and Gynecological Association. (1947) *President,* Paul Rollins, Seattle, Wash. *Secretary,* Clifford L. Fearl, 1133 S.W. Market St., Portland 1, Ore.

Philadelphia, Obstetrical Society of. (1868) *President,* Owen J. Toland. *Secretary,* John P. Emich, Jr., 155 W. Walnut Lane, Philadelphia 44, Pa. Meetings, first Thursday of the month, October through May.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President,* Henry W. Erving. *Secretary,* Joseph Loughrey, Medical Arts Bldg., Fifth and Atwood, Pittsburgh 13, Pa. Meetings, first Monday, October through May, except January.

Portland Society of Obstetricians and Gynecologists. (1928) *President,* William M. Wilson. *Secretary,* David W. James, 4212 N.E. Broadway, Portland 13, Ore. Meetings, fourth Wednesday, September through May.

Queens Gynecological Society. (1948) *President,* Joseph Rich. *Secretary,* B. Edmond Thomas, 30 Grace Ave., Great Neck, N. Y. Meetings, second Wednesday, October, December, February, and April.

Rochester Academy of Medicine, Obstetrics and Gynecology Section. (1939) *President,* Curtis Lund. *Secretary,* William Lange, 16 N. Goodman St., Rochester 7, N. Y. Meetings, as announced.

St. Louis Gynecological Society. (1924) *President,* Eugene G. Hamilton. *Secretary,* Ralph Woolf, 630 S. Kingshighway Blvd., St. Louis 10, Mo. Meetings, second Thursday, October, December, February, and April.

San Antonio Obstetrical and Gynecological Society. *President,* G. G. Passmore. *Secretary,* Frank M. Posey, Jr., 641 Moore Bldg., San Antonio, Texas. Meetings, second Wednesday of the month.

San Diego Gynecological Society. (1937) *President,* Wilton Lewis. *Secretary,* George Turner, 2330 First Avenue, San Diego 1, Calif. Meetings, last Friday of the month.

San Francisco Gynecological Society. (1929) *President,* Edmund F. Anderson. *Secretary,* Carl Goetsch, 2915 Telegraph Ave., Berkeley 5, Calif. Meetings, second Friday, September through April.

Seattle Gynecological Society. (1941) *President,* Paul Peterson. *Secretary,* L. Bruce Donaldson, 532 Stimson Bldg., Seattle 1, Wash. Meetings, third Wednesday, January, March, April, May, September, October, and November.

South Carolina Obstetrical and Gynecological Society. (1946) *President,* Lawrence L. Hester, Jr. *Secretary,* Albert J. Baroody, 352 W. Palmetto St., Florence, S. C. Next meeting, Fort Sumter Hotel, Charleston, S. C., Oct. 18 and 19, 1958.

South Dakota Society of Obstetrics and Gynecology. (1952) *President,* Paul Billingsley. *Secretary,* C. A. Stern, 1320 S. Minnesota Ave., Sioux Falls, S. D. Meetings, June and September.

Southern California, Obstetrical and Gynecological Assembly of. (1945) *President,* Daniel G. Morton, Los Angeles, Calif. *Secretary,* Keith P. Russell, 511 S. Bonnie Brae St., Los Angeles 57, Calif. Next meeting, Los Angeles, Feb. 9-13, 1959.

Southwest Obstetrical and Gynecological Society. (1951) *President,* Charles Van Epps. *Secretary,* Zeph B. Campbell, 550 W. Thomas Rd., Phoenix, Ariz. Next meeting, Phoenix, Ariz., Nov. 14 and 15, 1958.

Texas Association of Obstetricians and Gynecologists. (1930) *President,* Jesson L. Stowe, El Paso, Texas. *Secretary,* Oran V. Prejean, 1317 N. Washington Ave., Dallas 4, Texas. Annual meeting, February, 1959.

Tulsa County Obstetrical and Gynecological Society. (1955) *President,* Adolph N. Vammen. *Secretary,* James T. Maddox, Ranch Acres Medical Center, Tulsa, Okla. Five meetings per year.

Utah Obstetrical and Gynecological Society. (1948) *President,* Lindsay R. Curtis. *Secretary,* H. A. Theurer, Jr., 60 S. 4th East St., No. 8, Salt Lake City, Utah. Meetings second Thursday of October, December, February, and May.

Virginia Obstetrical and Gynecological Society. (1936) *President,* Paige E. Thornhill. *Secretary,* Brock D. Jones, Jr., 1204 Colonial Ave., Norfolk, Va. Meetings, April and October.

Washington Gynecological Society. (1933) *President,* Howard P. Parker. *Secretary,* Robert B. Nelson, Jr., 1824 Massachusetts Ave., N. W., Washington 6, D. C. Meetings, October, November, January, March, and May.

Washington State Obstetrical Association. (1936) *President,* Glen G. Rice. *Secretary,* Donald M. McIntyre, 1420 Seneca St., Seattle 1, Wash. Meetings, Spokane, Wash., Oct. 11, 1958, and Seattle, Wash., April 11, 1959.

West Texas Obstetrical and Gynecological Society. (1954) *President,* Joe L. Cornelison, San Angelo, Texas. *Secretary,* Tom C. Burditt, 1440 N. Third St., Abilene, Texas. Annual meeting in December.

Westchester Obstetrical and Gynecological Society. (1939) *President,* Douglas H. Robertson. *Secretary,* Joshua W. Davies, 28 Hobart St., Bronxville, N. Y. Meetings, second Wednesday, October, November, January, February, March, and May.

Wisconsin Society of Obstetrics and Gynecology. (1940) *President,* Ralph E. Campbell, Madison, Wis. *Secretary,* William C. Mussey, 113 N. Carroll Ave., Madison 3, Wis. Spring meeting in conjunction with the Wisconsin State Medical Society.